Perioperative temperature management for women undergoing caesarean section.

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Keywords

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Abstract

Background

Perioperative hypothermia is a significant problem for all surgical patients. All modes of anaesthesia (general, regional or neuraxial) adversely affect thermoregulation resulting in a subsequent temperature decline and resultant inadvertent hypothermia. Other surgical and environmental factors such as cool ambient operating theatre temperature and body exposure also contribute to heat loss. In addition to causing discomfort to surgical patients, particularly awake patients, perioperative hypothermia is associated with other, more serious, side effects including increased infection rates, increased blood loss, delayed wound healing and increased hospital stay.

Caesarean section is a common but major surgical procedure that is most often performed under neuraxial anaesthesia. In obstetric patients, perioperative hypothermia also has the potential to disrupt skin-to-skin contact and breastfeeding in the immediate postoperative phase. It is therefore imperative that measures are undertaken to reduce the occurrence of perioperative hypothermia as it is not only the mother, but also the newborn, that are adversely affected by the occurrence of this preventable condition. Current evidence-based guidelines for the prevention of perioperative hypothermia specifically exclude obstetric patients. This has left health care practitioners without clear evidence-based recommendations on which to base thermal care for this vulnerable population.

There are some special considerations that may partially explain the reluctance to include obstetric patients in these guidelines. These include the altered physiology that occurs with pregnancy, but also practical issues with methods of warming currently used in the general adult population. A further complication seen in this population is the influence of intrathecal (spinal) morphine, which is commonly administered for a greater duration of postoperative analgesia, but which intensifies temperature decline.

Aims

The overall aim of this research program was to establish effective treatment and management strategies for perioperative hypothermia for the obstetric population, to contribute to the knowledge base for future guideline, policy and care planning.

Methods

This research program was conducted in three phases:

1. A systematic review of the effectiveness of current evidence to prevent and treat perioperative hypothermia specifically for caesarean section patients. This was based upon a published protocol. Search strategies aimed to identify both published and unpublished literature in all languages, and searches were complete to May 2012. Two independent reviewers (with a third where consensus was needed) utilised Joanna Briggs Institute MASTARI critical appraisal methods, narrative analysis and meta-analysis using Rev-Man software. Recommendations for both practice and further research were generated, based upon the review results, and attributed a JBI Level of Evidence.

2. A retrospective, case-control study was conducted from May 2013-May 2014 to further examine temperature decline between both women receiving intrathecal morphine, and not receiving intrathecal morphine, for emergency or elective caesarean section. Two researchers collected data from 358 charts. Data analysis included logistic regression to predict the outcome of hypothermia across the population. Inter-rater reliability was determined using the kappa statistic.

3. A pragmatic, single-blinded, randomised controlled trial of the effectiveness of a preoperative warming regime for women receiving intrathecal morphine for elective caesarean section was conducted from February 2015- February 2016, in 50 healthy women. Computer-generated randomisation was used to allocate participants to either the usual care group, or the intervention group who received 20 minutes of preoperative forced air warming. The primary outcome of maternal temperature change was assessed via aural canal and bladder temperature measurements at regular intervals. Secondary outcomes included maternal thermal comfort, shivering, mean arterial pressure, agreement between aural and bladder temperature, and

neonatal outcomes (axillary temperature at birth, Apgar scores, breastfeeding and skin-to-skin contact). Data was analysed using SPSS™ 22 and MedCalc™ software.

Results

The first phase of the research program (the systematic review) found that intravenous fluid warming is effective at maintaining maternal temperature, and reducing shivering, however does not improve maternal thermal comfort or neonatal temperature. Warming devices, comprising of either under body or over body upper body forced air warming, were effective at preventing hypothermia and this effectiveness increased if forced air warming was applied preoperatively. Preoperative active warming also decreased shivering and improved neonatal temperature, however did not improve Apgar scores. Leg wrapping was not effective at maintaining maternal temperature. The review also identified that warming was less effective in the studies where intrathecal morphine was administered.

The second phase of the research program (the retrospective, case-control study) found that there was statistically significant temperature decline across the whole population of women receiving spinal anaesthesia for caesarean section, whether or not they received intrathecal morphine (0.62°C, 95% CI 0.54-0.69) $p<0.001$, $t(291) = 16.7$). The subset of women that experienced the phenomenon of profound and prolonged intrathecal morphine related hypothermia could not be explored further due to a low identification of this condition (2% of the study population), however results indicated that temperature decline with either fentanyl or morphine was not dose-related. In addition, level of block did not influence hypothermia, but emergency surgery, pregnancy-induced hypotension and increased Body Mass Index were found to be protective factors regarding the risk of developing perioperative hypothermia.

The third phase of the research program revealed no significant difference in aural temperature change from baseline to the end of the procedure between groups when examined using a general linear model with the Intention to Treat principle, and with adjustment for baseline temperature and surgery duration: $F(1, 47) = 1.2$, $p = 0.28$, partial eta squared = 0.03. An exploratory analysis of secondary outcomes indicated that there were no statistically significant differences between groups in any of the

secondary outcomes, except in post-spinal mean arterial pressure (Md=89, n =25 in the control group versus Md=85, n=25 in the intervention group, U = 248.5, z =2.36, p=0.03) although this difference had limited clinical significance.

Conclusion

Maintaining temperature and reducing temperature decline in the population of women undergoing caesarean section, particularly those receiving intrathecal morphine, is challenging. Based upon this research, some recommendations that currently apply to the general adult population can be extended to the obstetric population, however it appears that single interventions alone may be insufficient to reduce perioperative hypothermia in women receiving neuraxial anaesthesia. Women who receive intrathecal morphine may experience less benefit seen from conventional warming methods, in comparison to other populations. Warming appears to be well tolerated by obstetric patients. Evidence from this research program can be used by health care organisations to develop evidence-based guidelines for the surgical thermal care of obstetric patients. This will help to establish standards of care, assisting in the ultimate goal of reducing perioperative hypothermia for women undergoing caesarean section.

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Publications and presentations

Publications

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List of Abbreviations

ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CS	Caesarean section
IPH	Inadvertent perioperative hypothermia
IV	Intravenous
OR	Operating Room
PACU	Post Anaesthetic Care Unit
RCT	Randomised controlled trial
SPSS	Statistical Software for Social Sciences

Statement of Original Authorship

The work contained in this thesis has not been previously submitted to meet requirements for an award at this or any other higher education institution. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made.

Signature: 

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Chapter 1: Introduction

1.1 INTRODUCTION

Temperature decline and subsequent heat loss during surgery is associated with numerous undesirable side effects with potentially serious complications for the surgical patient (NCCNSC 2008). Obstetric patients undergoing caesarean section are particularly vulnerable to heat loss and unintentional perioperative hypothermia related to the length of surgery, the amount of body surface exposure, and the predominant use of neuraxial anaesthesia. Inadvertent perioperative hypothermia is largely preventable with adequate care planning in reference to published guidelines (NCCNSC 2008); however, current evidence-based guidelines for the prevention of perioperative hypothermia specifically exclude obstetric patients. This leaves health care practitioners without clear evidence-based recommendations on which to base thermal care for this vulnerable population. This chapter will provide context for the thesis by presenting a brief background on the key concepts related to the problem of perioperative hypothermia in obstetric patients. This will be followed by an outline of the aims of the research program as well as the scope and significance of the program. The chapter will conclude with an outline of the thesis.

1.2 PERIOPERATIVE HYPOTHERMIA

Inadvertent perioperative hypothermia, generally defined as the unintentional cooling of the body's core temperature below 36°C (NCCNSC 2008) related to undergoing a surgical procedure, is associated with numerous side effects that are undesirable and best avoided in the postoperative patient. As well as causing general discomfort for patients, other complications include (but are not limited to) increased blood loss (Rajagopalan, Mascha, Na, & Sessler, 2008), higher wound infection rates (Kurz, Sessler, & Lenhardt, 1996), suppressed immune function (Beilin et al., 1998), increased hospital stay (Kurz, et al., 1996) and greater hospital costs (Mahoney & Odom, 1999). Both general and neuraxial anaesthesia, as well as external, environmental and surgical factors, contribute to the heat loss that patients can experience when they undergo most surgical procedures. Rates of inadvertent perioperative hypothermia remain high, at between 50-54% for general adult surgical

populations (Hooven, 2011; Munday, Hines, & Chang, 2013), but as high as 80% in caesarean section patients receiving spinal anaesthesia (Chakladar & Harper, 2010). These rates are unacceptably high and perioperative hypothermia is largely avoidable.

The recognition that impaired thermoregulation results from anaesthesia and surgery, and the direct adverse impact that impaired thermoregulation has upon a host of patient outcomes, has steadily increased over the last 25 years. Much of the early knowledge around this topic can be attributed to Daniel Sessler and his colleagues (Sessler, 1993). All modes of anaesthesia (general, regional or neuraxial) influence the thermoregulatory system. Environmental and surgical factors also contribute to heat loss. The cool ambient temperature of operating theatres, body exposure, fluid and blood loss, as well as preoperative fasting requirements are all contributory factors to perioperative heat loss (NCCNSC 2008).

Prevention of perioperative hypothermia is multi-faceted and requires consistent vigilance on the part of health care providers. Risk factor tools and evidence-based guidelines are available for health care providers to, firstly, assist in the prevention of perioperative hypothermia, but also secondly, to assist in the management of the condition once it occurs (Association of Operating Room Nurses ARP Committee, 2007; Hooper et al., 2010; NCCNSC 2008). The most comprehensive, and widely cited, guideline available to date was developed by the National Collaborating Centre for Nursing and Supportive Care (NCCNSC) for the National Institute for Health and Care Excellence in 2008 (NCCNSC 2008). Obstetric patients were notably excluded from these internationally recognised guidelines at their initial development. Subsequent reviews of the guidelines have again failed to integrate recommendations for obstetric patients (National Institute for Health and Care Excellence 2015). There has also been a lack of synthesized evidence for perioperative hypothermia prevention for obstetric patients, leaving health care providers without clear evidence-based guidance on the appropriate methods of preventing this adverse and uncomfortable condition.

1.3 CAESAREAN SECTION

Caesarean section refers to the operative delivery of the baby via a surgical incision in the mother's abdomen. It is undertaken for many varying reasons such as where vaginal delivery may be complicated, inadvisable or in emergency circumstances, for both the health of the mother and/or baby. In Australia, caesarean section delivery occurs in approximately 1 in 3 births, with 95894 caesarean section deliveries occurring in Australia in 2011, accounting for 32% of births (Australian Institute of Health and Welfare 2014, 2014).

Caesarean section is, in most cases, performed under neuraxial (epidural or spinal) anaesthesia, which provides women with the opportunity to be awake for the delivery of the baby. Neuraxial anaesthesia also reduces the risks from general anaesthesia, which is generally only performed when there is deemed to be clinical need related to co-existing morbidity (Hughes, Levinson, Rosen, & Shnider, 2002), or maternal preference. Common side effects from neuraxial anaesthesia include hypotension and itching. Furthermore, neuraxial anaesthesia impairs thermoregulation resulting in heat loss (Sessler, 2008). In addition, heat loss in caesarean section patients is also influenced by pregnancy-associated vasodilation (Dunn, York, Cheek, & Yeboah, 1993), relatively large amounts of blood and fluid loss, and a high degree of body exposure needed to access the surgical site. These factors, alongside impaired thermoregulation from neuraxial anaesthesia, increase the vulnerability of women undergoing caesarean section to develop perioperative hypothermia. Spinal opioids are commonly given to enhance analgesia during surgery, and to prolong postoperative pain relief (Hess, Snowman, & Wang, 2005; Hughes, et al., 2002). However, some women that receive intrathecal morphine develop particularly prolonged hypothermia with paradoxical symptoms of diaphoresis and feeling hot (Hess, et al., 2005; Ryan, Price, Warriner, & Choi, 2012). For these women, conventional warming methods are not as effective or appropriate as when used to treat the more common perioperative hypothermia usually experienced. Furthermore, intrathecal morphine use is a key differential between studies that have found varying levels of effectiveness of warming for women undergoing caesarean section (Halloran, 2009).

1.4 PERIOPERATIVE HYPOTHERMIA PREVENTION FOR OBSTETRIC PATIENTS

Methods of warming recommended for general surgical populations include both passive and active strategies. Active warming, which includes forced air warming, intravenous fluid warming and heated mattresses, has shown more effectiveness at reducing temperature decline than passive warming, which revolves around the use of warmed cotton blankets or reflective coverings (Moola & Lockwood, 2011; NCCNSC 2008).

The use of active warming interventions for caesarean section has been reported to be as low as 16% (Woolnough, Hemingway, Allam, Cox, & Yentis, 2009) and 18% (Aluri & Wrench, 2014) in the UK, however its use in Australia for obstetric patients has not yet been quantified. Primary research of the use of warming strategies to prevent perioperative hypothermia in the caesarean section population varies in relation to results, quality and usefulness. The effectiveness of forced air warming, which is recommended by NICE for general adult populations (NCCNSC 2008) has varied between studies (Fallis, Hamelin, Symonds, & Wang, 2006; Horn et al., 2002). Furthermore, questions have been raised about the practicality of over body forced air warming strategies, and the tolerability of warming, for obstetric patients (Chakladar & Harper, 2010; Petsas, Vollmer, & Barnes, 2009). In addition, warming strategies have been less effective in studies where intrathecal morphine has been administered (Halloran, 2009). Nevertheless, due to the adverse side effects, discomfort and disruption for women undergoing caesarean section caused by perioperative hypothermia, it is imperative that effective methods of preventing this condition are identified.

1.5 RESEARCH AIMS

The starting point for this research program was to address the deficit of evidence based recommendations for maternal thermal care by undertaking a systematic review of the current evidence of effectiveness of interventions to prevent or manage hypothermia experienced by women undergoing caesarean section. From this work, a gap in the evidence surrounding temperature decline, and the effectiveness of warming interventions, in the specific group of women receiving intrathecal

morphine for caesarean section was identified. This provided the impetus for the subsequent two phases of the research program; an observational study, and a pragmatic, randomised controlled trial. Therefore, the aims of this research program were as follows:

1. To review existing evidence regarding the effectiveness of interventions to prevent or manage hypothermia experienced by women undergoing caesarean section (by systematic review)

2. To investigate temperature decline and hypothermia related to intrathecal morphine, and identify the subset of women experiencing profound and problematic hypothermia related to intrathecal morphine (via retrospective case-control study)

3. To test a preoperative warming regime to reduce temperature decline in women receiving intrathecal morphine for caesarean section (via randomised controlled trial).

1.6 SIGNIFICANCE AND SCOPE OF THE RESEARCH PROBLEM

The lack of evidence-based recommendations to encompass or specifically address obstetric patients means that there has been no clear directives for health care providers to follow, a lack of clarity surrounding which methods of prevention are both effective or appropriate, and therefore a danger that this patient group will be neglected, resulting in high rates of unintended perioperative hypothermia. The systematic review of the experimental evidence on the prevention and management of perioperative hypothermia synthesised the available evidence, and generated evidence-based recommendations that could be applied specifically to this population. This systematic review also highlighted gaps in the evidence, and raised the question as to whether warming interventions are as effective, and whether hypothermia is exacerbated, in patients that receive intrathecal morphine during spinal anaesthesia (which in many institutions is standard care) (Cobb, Cho, Hilton, Ting, & Carvalho, 2016) for caesarean section.

To partially address this question, a retrospective case control study aimed to compare heat loss and hypothermia between women undergoing caesarean section

both with and without intrathecal morphine. After establishing that there was significant temperature decline experienced across the population of women undergoing caesarean section, whether or not they received intrathecal morphine, and identifying that there was a gap in the science regarding whether preoperative warming is effective for women who receive intrathecal morphine for caesarean section, a pragmatic randomised controlled study was conducted to test this intervention. Preoperative warming has been shown to have benefit at reducing temperature decline in many populations (Andrzejowksi, Hoyle, Eapen, & Turnbull, 2008) and is recommended by NICE for general adult surgical patients (NCCNSC 2008), however in the obstetric population had only been tested where women had not received intrathecal morphine, which provides effective postoperative analgesia, but which is associated with a number of side effects such as pruritus, nausea and vomiting, respiratory depression and impaired thermoregulation. Therefore, the randomised controlled study aimed to test a feasible period of active preoperative warming in this population. In this research program, inadvertent perioperative hypothermia is categorised as a temperature <36.0°C, based upon the common cut-off cited in the most up-to-date literature (NCCNSC 2008).

1.7 OUTLINE OF THESIS

This thesis presents the three phases of the research program as a series of published, accepted and submitted publications, each contributing to new knowledge for the prevention of perioperative hypothermia for women undergoing caesarean section.

Chapter 2 reviews the literature to establish the basis for this research program, including the existing literature surrounding perioperative hypothermia, and specifically the relevance and treatment of the condition for caesarean section patients. This chapter informs the work in the subsequent chapter and, in particular, the development of the systematic review in the following chapter.

Chapter 3 presents phase one of the research program: a systematic review of the evidence of effectiveness of interventions to assist perioperative temperature management for women undergoing caesarean section. The shortened version of this

systematic review, published in Worldviews on Evidence Based Nursing, which focuses on the primary outcome of maternal temperature, is included in this chapter.

Chapter 4 includes the secondary outcomes from the full systematic review, published in the JBI Database of Systematic Reviews and Implementation Reports, namely shivering, maternal thermal comfort, length of Post Anaesthetic Care Unit (PACU) stay, neonatal temperature at birth, Apgar scores and umbilical pH. The full review is included in Appendix A.

Chapter 5 includes phase two of the research program, an observational study of hypothermia and temperature decline in women receiving intrathecal morphine for caesarean section, and presented as the paper accepted for publication in the Journal of PeriAnesthesia Nursing.

Chapter 6 reports phase three of the research program, a randomised controlled trial of the effectiveness of a prewarming regime to prevent maternal temperature decline in women receiving intrathecal morphine for caesarean section, as the paper submitted for publication.

Chapter 7 is the discussion of the overall findings of the research program in the context of current evidence, the significance of the findings and recommendations for practice.

Finally, Chapter 8 presents the conclusions of the research program and presents areas for further research.

Additional information related to the three phases of the research program, including but not limited to, data collection forms and ethics approvals as well as the full JBI version of the systematic review, are included as appendices.

Chapter 2: Background and Literature Review

2.1 INTRODUCTION

Inadvertent perioperative hypothermia is generally defined as the unintentional cooling of the body's core temperature below 36°C (NCCNSC 2008) related to undergoing a surgical procedure. The association of inadvertent perioperative hypothermia with numerous adverse effects for surgical patients (NCCNSC 2008) is well documented (as reported in Chapter 1). Inadvertent perioperative hypothermia is a common problem for patients undergoing caesarean section (Chakladar & Harper, 2010). The rate of hypothermia, if not managed, for women undergoing caesarean section under spinal anaesthesia has been estimated as being as high as between 32% (Hess, et al., 2005) and 80% (Chakladar, Dixon, & Harper, 2011). Similarly, the rate of hypothermia in general surgical adult populations has also been found to be high, at around 50-54% (Hooven, 2011; Munday, Hines, & Chang, 2013).

Caesarean section is a major surgical procedure and can involve relatively large amounts of blood and fluid loss, which increases the vulnerability of women undergoing caesarean section to developing hypothermia. A high degree of body exposure is required during caesarean section in order to access the surgical site and heat loss results from the exposed skin and body cavities (Dunn, et al., 1993). In many cases, women await surgery in cool waiting areas wearing thin surgical gowns. The patient's preoperative thermal status also influences heat loss and their progression to hypothermia. In addition, pregnancy associated vasodilation (Dunn, et al., 1993) also contributes to core heat loss, promoting the loss of heat from the body's core compartment to the peripheries. This effect is also heightened by vasodilation related to anaesthesia. Regional anaesthesia is, in most cases, the anaesthetic mode of choice for caesarean section surgery (Fallis, et al., 2006) but may also be an aggravating factor for the development of hypothermia (Frank, El-Rahmany, Cattaneo, & Barnes, 2000) by inhibiting normal thermoregulation, particularly when opioids are used (Hess, et al., 2005). Effective prevention or treatment for inadvertent perioperative hypothermia in this group of patients has not

yet been definitively established, which has provided the impetus for this research program.

2.2 THERMOREGULATION

Core temperature, in all humans, is maintained only within very narrow limits (Sessler, 2000) via a system of afferent and efferent signals and the hypothalamus. Normally core temperature is maintained between 36.5-37.5°C. The body depends upon this narrow range for normal functioning to occur (Insler & Sessler, 2006). Core temperature, as differentiated from peripheral temperature (which varies more widely), refers to the temperature of the body's core compartment. This is comprised of tissues that are well-perfused and of higher uniform temperature than the remainder of the body (Insler & Sessler, 2006). Although these temperatures do fluctuate according to circadian rhythm and, in females, according to the menstrual cycle (Bicalho, Viana Castro, Cunha Cruvinel, & Bessa Jr, 2006) (Kurz, 2008), core body temperature has been described as 'one of the most tightly regulated parameters of human physiology' (Kurz, 2008)[p627] and also as the 'best single indicator of thermal status in humans' (Sessler, 2008)[p318].

A three stage system of thermoregulation has been acknowledged (Bicalho, et al., 2006). Afferent signals are sent from the skin, deep tissues and spinal cord to the central nervous system (stage one), the hypothalamus centrally processes these signals (stage two) and then sends efferent signals to adjust temperature (by either an increase or decrease) (stage three). Simply described, if the hypothalamus detects a deviation in temperature level then it sends an appropriate response to either increase heat loss (for example, sweating) or decrease heat loss (for example, vasoconstriction and shivering), thus returning thermal balance. The space or range between the 'too hot' and 'too cold' response (called the inter-threshold range) is generally just 0.4°C (Buggy & Crossley, 2000). Thus, temperature control is a very fine balance.

Generally, the body also generates heat by various methods: basal metabolic rate (generated by the body's maintenance of normal functions), thermogenesis (generated from food digestion), physical activity (absent during anaesthesia) and hormonal influences (Insler & Sessler, 2006). At any time, the human body can lose or gain heat via four mechanisms; radiation (for example, when heat is lost between the body and the cooler ambient environment of the operating theatre), conduction

(for example when heat is lost between skin and cooler linen), convection (such as heat loss between exposed skin and the cooler ambient environment) and evaporation (such as heat loss from exposed body cavities) (Buggy & Crossley, 2000; Dunn, et al., 1993; Sarti, Recanati, & Furlan, 2005).

Thermoregulatory shivering as a response to cold, characterised by involuntary activities or tremor of muscles, increases metabolic heat production (Insler & Sessler, 2006) but can also be an unpleasant and uncomfortable experience for patients. The core thermoregulatory threshold for shivering is normally 35.5°C (Insler & Sessler, 2006; Kurz, 2008) and its presence may, therefore, be an indication of a 'too cold' thermal response; however shivering, in some instances, is thought to be non-thermoregulatory. Efferent responses to cold include vasoconstriction and, as described above, shivering. Vasoconstriction occurs more widely and regularly than shivering and works to reduce heat lost through the mechanisms of radiation and convection (Kurz, 2008), by reducing blood flow particularly to the extremities. Both warm and cold receptors are situated all over the body (Kurz, 2008), however humans have many more cold receptors than warm receptors (Buggy & Crossley, 2000; Insler & Sessler, 2006) and thus, peripheral thermoregulatory responses are geared towards detecting cold rather than warmth (Insler & Sessler, 2006).

Behavioural influences on thermoregulation (such as the ability to add or remove extra clothing, or take other cooling or warming measures as necessary) have been described as 'quantitatively more important' (Buggy & Crossley, 2000)^{p615} than autonomic responses in terms of temperature regulation. In unanaesthetised patients, impulses sent by the hypothalamus to the cerebral cortex, cause behavioural responses (such as adding clothing as described above) (Buggy & Crossley, 2000), but in anaesthetised patients the ability to use behavioural means of temperature control are impaired, if not altogether absent.

2.3 THERMOREGULATION AND ANAESTHESIA

General, regional and neuraxial anaesthetics all have an influence on the thermoregulatory system, albeit in slightly varying ways. Regional or neuraxial anaesthetics (either epidural or spinal or combined spinal-epidural) are the common modes of anaesthesia for women undergoing CS, as compared to general anaesthesia.

These modes of anaesthesia are beneficial in terms of both maternal and anaesthetic preferences. From a maternal perspective, neuraxial anaesthesia provides the opportunity to stay awake during surgical delivery (Hughes, et al., 2002). From an anaesthetic perspective, avoiding general anaesthesia minimises the risk of airway management issues and of drug depression for the newborn baby (Hughes, et al., 2002). The choice of anaesthetic depends on the urgency of the surgery (not only emergency versus elective, but also the degree of emergency), preferences of both the mother and anaesthetist, and anaesthetic judgement (based on safety and comfort for the mother, as well as providing the best working conditions for the surgeon) (Hughes, et al., 2002).

In all surgical procedures, external and surgical factors combine with anaesthetic related autonomic temperature control impairment to influence the degree of heat loss experienced. External factors such as the requirement for patients to wear thin surgical gowns, remain nil by mouth and often experience prolonged preoperative waiting periods are also of relevance to obstetric surgical patients, and can impair thermal status (NCCNSC 2008). During anaesthesia, the inter-threshold range is thought to increase, whilst responses to maintain heat are decreased. During regional anaesthesia, there is as much as a three-fold increase from the normal inter-threshold range (or thermoneutral zone), which is therefore widened (Kurz, 2008). Skin temperatures in blocked areas may be misinterpreted as elevated by the central thermoregulatory system (Kurz, Sessler, Narzt, Lenhardt, & Lackner, 1995). The shivering threshold is reduced (Kurz, 2008) and the reduced gain of shivering above the level of the block (Buggy & Crossley, 2000) does not compensate for the lack of shivering below the level of the block.

During neuraxial anaesthesia, central thermoregulation and peripheral thermoregulation are both adversely effected (Kurz, 2008). A three stage process of heat loss (or redistribution of heat) is described during neuraxial anaesthesia (Sessler, 2000): firstly heat redistributes from the core to the peripheries (similar as occurs during general anaesthesia,) caused by vasodilation of the anaesthetised section of the body. This 1-2°C loss typically occurs during the first hour. Secondly, vasoconstriction loss in the anaesthetised sections of the body decreases the efficiency of heat maintenance. Thirdly, there is a decrease in the vasoconstriction and shivering thresholds even in non-anaesthetised areas (Bicalho, et al., 2006;

Sessler, 2000). Interestingly, patients may experience a sense of thermal comfort or warmth after initiation of regional anaesthetic blocks, possibly due to the lack of skin temperature detection below the level of the block being misinterpreted as warmth (Kurz, 2008).

2.4 DETECTION OF HYPOTHERMIA

The early detection or identification of hypothermia and decreased thermal status can facilitate action to prevent further deterioration. Preoperative thermal status influences the degree to which core-periphery heat redistribution will occur (Arkilic, Akca, Taguchi, Sessler, & Kurz, 2000). Preoperative fasting, the requirement to wear thin hospital gowns during the preoperative wait, and the administration of preoperative medications notably sedation, contribute to reduced temperatures in patients when they arrive in the perioperative suite. Knowledge of the patient's preoperative thermal status is vital when planning perioperative care and this expectation has been reflected in guidelines relating to perioperative management of hypothermia for all surgical (non-obstetric) patients (Hooper, et al., 2010; NCCNSC 2008). Risk factor tools are available to assist in the identification of patients at high risk of developing hypothermia (Hooper, et al., 2010; NCCNSC 2008) so that measures to safeguard normothermia in the operating suite can be put into place. These risk factor tools are however generalised to adult patient groups only and have not been promoted for use in obstetric surgical patients. In fact, the evidence-based guidelines, The Management and Prevention of Inadvertent Perioperative Hypothermia, developed by the National Institute for Clinical Health and Excellence (NICE) in the UK actually exclude pregnant patients from the guideline (NCCNSC 2008). Experts argue that these could be potentially transferable to obstetric patients as guidelines are needed for this group of patients (Chakladar & Harper, 2010). A number of systematic reviews (Galvao, Liang, & Clark, 2010; Moola & Lockwood, 2011) have scrutinised the management of perioperative hypothermia using various interventions but these have largely overlooked obstetric patients as a distinct and particularly vulnerable group.

Hypothermia during neuraxial anaesthesia is often not detected until patients reach the Post Anaesthetic Care Unit (PACU). A study of temperature monitoring and management found that there is a lack of temperature monitoring during neuraxial anaesthesia (Arkilic, et al., 2000) as it is often not considered a necessity by

anaesthetists (Arkilic, et al., 2000). Others have confirmed that temperature monitoring is indeed often overlooked, perhaps due to the lack of an optimum monitoring site or because malignant hyperthermia, a separate serious perioperative complication, is not a risk factor with neuraxial anaesthesia (Frank, et al., 2000) (and therefore the perceived importance of temperature monitoring is decreased). In reality temperature should be monitored routinely (Arkilic, et al., 2000), in order to detect temperature variations as they occur. Expert opinion suggests that core temperature should indeed be measured in patients undergoing neuraxial anaesthesia, particularly those undergoing major surgery (Lenhardt, 2003) or surgery involving the body cavities (Sessler, 2008) which would therefore include caesarean section. In addition, patient detection of heat loss is also impaired during anaesthesia so they may not initially perceive the heat loss due to impaired thermoregulation and detection of lower temperatures (Insler & Sessler, 2006). The apparent lack of monitoring temperature intraoperatively means that hypothermia becomes more a problem to treat rather than prevent, in many cases, resulting in a reactive rather than proactive approach. In this respect, it becomes the responsibility of nurses caring for these patients postoperatively to resolve the hypothermia. Prevention of perioperative hypothermia was rated as one of the top ten priorities (eighth out of 10 priority issues) by a recent survey of perioperative nurses regarding patient safety issues, however only 31% (966) of 3137 respondents rated it as a high priority (Steelman & Graling, 2013) and it was suggested that nurses at the front line of direct patient care were more likely to recognise the need for a focus on this aspect of care.

Temperature monitoring can occur at many different sites: whilst a handful of these sites are considered to be indicative of true core temperature, a number of other sites offer a ‘near-core’ reading. These ‘near-core’ sites are generally easier from which to obtain readings. The gold standard of core temperature measurement is the use of the pulmonary artery, however other core sites include the tympanic membrane, distal oesophagus and nasopharynx (Sessler, 2008). Near-core sites, such as the oral cavity, axilla, bladder, rectum and skin-surface, can be used to given an indication of core temperature however there are also limitations associated with these methods, often related to accuracy. In such a tightly regulated parameter as human thermal status, the influence of inaccurate measurement can be magnified. A suggested rule of thumb for the combined inaccuracy of a temperature measurement site or device,

is that this should not exceed 0.5°C (Sessler, 2008). Both in clinical practice and clinical research, it is therefore imperative that careful consideration is given to the mode of temperature measurement used.

During neuraxial anaesthesia for caesarean section surgery, more invasive methods of temperature measurement (such as pulmonary artery or oesophageal) are extremely unlikely to be utilised, however bladder measurements is possibly a more feasible and less disruptive option (as bladder catheterisation is necessitated during caesarean section surgery). As discussed earlier, it also appears to be common practice for temperature measurement during neuraxial anaesthesia to be neglected completely. A balance between patient comfort and an acceptable level of device accuracy seems desirable.

2.5 ADVERSE OUTCOMES RELATED TO PERIOPERATIVE HYPOTHERMIA

Whilst all patients are at risk of perioperative hypothermia and the associated side effects, these effects of hypothermia can be especially serious for women undergoing caesarean section and their newborns, notwithstanding the discomfort and inconvenience resulting from hypothermia that requires treatment.

Postpartum haemorrhage is a serious postpartum concern for caesarean section patients and therefore, the avoidance of risk factors that can increase blood loss, such as hypothermia, should be undertaken. A meta-analysis of fourteen published randomised controlled trials relating to blood loss and ten published randomised controlled trials relating to transfusion requirements, has revealed that even mild hypothermia increases blood loss and transfusion requirements (Rajagopalan, et al., 2008). Although there was a limited search strategy (searching for published studies only) and a limited quality appraisal system used for this meta-analysis, the results remain of interest. Normothermia was found to be associated with lower blood loss than hypothermia. Blood loss is estimated to increase by around 16% with mild hypothermia and the relative risk of blood transfusion is increased by around 22% with mild hypothermia (Rajagopalan, et al., 2008).

The detrimental effects of hypothermia also extend to wound healing. Hypothermia has been linked with delayed wound healing and increased wound infection rates in

some surgical patient groups, such as colo-rectal surgery (Kurz, et al., 1996). Indeed, it has been indicated that perioperative hypothermia can suppress immune function (Beilin, et al., 1998). Although, conversely, two retrospective case-control studies (Edwards, Madani, & Duff, 2003; Munn, Rouse, & Owen, 1998) failed to find an association between perioperative hypothermia and wound infection, these studies both have limitations, not least in the use of postoperative temperature readings as an indicator of intraoperative hypothermia (rather than the use of intraoperative readings) (Munn, et al., 1998). A systematic review of 26 intraoperative warming randomised controlled trials to prevent postoperative complications (Scott & Buckland, 2006) favoured the use of warming to reduce wound infections, but the search strategy utilised during this review was limited in its breadth and completeness of searches. No unpublished literature was sought, thus increasing the risk of publication bias. In addition, although a description of quality indicators used to select studies is provided, it is unclear if a validated tool was utilised for critical appraisal. Of the 26 included studies, 17 did not have a clear randomisation process described: therefore, there is some question of the quality of the studies included in this review, and therefore the validity of the results.

Greater morbidity, whether directly or indirectly associated with inadvertent perioperative hypothermia, would be expected to lengthen hospital stay. Indeed, the occurrence of inadvertent perioperative hypothermia has been linked with increased duration of hospital stay, in a randomised controlled trial of 200 patients undergoing colorectal surgery which investigated the effects of normothermia versus hypothermia in relation to surgical wound infection and duration of hospitalization (Kurz, et al., 1996). In addition to the possible benefits that normothermia affords patients in relation to lower incidence of post-surgical wound infections, patients remaining normothermic had shorter hospital stays (Kurz, et al., 1996) even amongst those who had no infection. However, temperatures of the hypothermic group in this study were kept at 34.5°C, which may be considered more extreme than the milder hypothermia experienced by most patients experiencing inadvertent perioperative hypothermia. In addition, it appears that postoperative temperature was not monitored or controlled for, therefore introducing the potential for confounding the study results.

Inadvertent perioperative hypothermia may also result in increased Post Anaesthetic Care Unit stay (PACU) (Lenhardt et al., 1997). A prospective randomised controlled trial found that hypothermic patients reached fitness to discharge from PACU approximately 40 minutes later than normothermic patients undergoing major abdominal surgery (Lenhardt, et al., 1997), even if core temperature was not included as part of a discharge criteria. This suggests that, aside from the time, resources and cost factors associated with rewarming hypothermic patients to meet temperature related discharge criteria, hypothermia can also affect the overall recovery of patients in other aspects. Inadvertent perioperative hypothermia has also been shown to increase duration of effect of certain medications, such as muscle relaxants (Heier & Caldwell, 2006; Leslie, Sessler, Bjorksten, & Moayeri, 1995), with the duration of neuromuscular blockade doubling with a 2°C drop in temperature (Heier & Caldwell, 2006), which can also impact on duration of time spent in the perioperative suite.

Taking the above factors into consideration, it is not surprising that inadvertent perioperative hypothermia has been linked with increased costs by a meta-analysis examining the costs of maintaining normothermia (Mahoney & Odom, 1999) balanced with outcomes across varying patient groups. The authors found that an average temperature drop of 1.5°C resulted in hospital costs between US$2500-7000 resulting from adverse outcomes. However, this meta-analysis, apparently conducted without a rigorous critical appraisal to determine the quality of included studies, has not been updated since first publication in 1999. With the volume of literature and new knowledge acquired since this date, updated analysis would be worthwhile. As health care providers seek to improve efficiency and meet the increasing demands for services, it becomes even more vital that the reduction of preventable adverse patient outcomes is prioritised. At the very least, awareness of perioperative normothermia should be promoted to identify and alleviate hypothermia related patient discomfort for all patients.

As well as the discomfort from perceived cold, shivering, accompanying decreased thermal status, has been reported to be a source of distress to women undergoing caesarean section (Liu & Luxton, 1991; Roy, Girard, & Drolet, 2004), in a randomised double-blind study of the effect of prophylactic epidural fentanyl administration upon shivering (Liu & Luxton, 1991), and a prospective double-blinded randomised controlled trial of intrathecal meperidine to reduce shivering

(Roy, et al., 2004). The latter study found that intrathecal meperidine reduced the incidence and intensity of shivering, but the optimal dose was not established. It also appears that intraoperative shivering only was investigated; therefore questions remain as to the incidence of postoperative shivering. Liu and Luxton's study of epidural fentanyl administration found that shivering was reduced in the intervention group (Liu & Luxton, 1991), however fentanyl non-shiverers also experienced the largest decrease in mean axillary temperature.

Shivering may also interfere with patient monitoring (Liu & Luxton, 1991), impairing the ability of devices to obtain readings due to patient movement. It is especially important that pre-emptive measures are taken to reduce shivering, associated with perioperative hypothermia, during caesarean section as it may impair the mother's ability to hold her newborn (Leslie & Sessler, 2003) (both immediately post-delivery and in the recovery room) and also postoperatively (Butwick, Lipman, & Carvalho, 2007) when it can interfere with bonding and the instigation of breastfeeding. These factors can adversely affect maternal experience and satisfaction with care. In addition, particularly disruptive shivering may be sufficient to disrupt the surgical procedure (Leslie & Sessler, 2003).

The adverse effects of inadvertent perioperative hypothermia are not limited to the mother alone. Fetal temperature is related to, and usually slightly higher than, maternal temperature (Butwick, et al., 2007) and thus, the baby's temperature also alters, as the mother's temperature decreases (or increases). Discrepancies between what is considered normal newborn temperature exist due to disagreements in literature and textbooks with inadequate referencing to support provided figures (Takayama, Wang, Uyemoto, Newman, & Pantell, 2000) but a recent study of full term infant's medical records found that mean axillary temperature was 36.5°C (Takayama, et al., 2000), whereas 36.5°C has been previously cited as a lower limit of newborn temperature (Takayama, et al., 2000). The authors argue that normal newborn temperature needs to be redefined, citing their results to support the assertion that normal newborn temperature may be lower than previously thought.

2.6 TREATMENT AND PREVENTION FOR INADVERTENT PERIOPERATIVE HYPOTHERMIA FOR CAESAREAN SECTION PATIENTS

Women undergoing caesarean section have been neglected in evidence-based recommendations and guidelines developed to enhance perioperative care and reduce hypothermia for surgical patients. This is evident in the explicit exclusion of pregnant patients from the widely recognised NICE guidelines on inadvertent perioperative hypothermia (NCCNSC 2008). The lack of guidance has potentially left this patient group at risk of being overlooked in regard to implementing regimes designed to protect perioperative patients against inadvertent perioperative hypothermia in practice. This is unfortunate, not least because the thermal status of the mother is also linked to the thermal status of the newborn baby; thus, it is not only the mother in isolation that may suffer from the occurrence and adverse effects of inadvertent perioperative hypothermia. As Baker and Lawson emphasise in a retrospective chart review of maternal and newborn outcomes related to perioperative hypothermia in elective low-risk caesarean section births, 'every effort should be made to prevent hypothermia in both mother and newborn' (Baker & Lawson, 2012) despite this study failing to find a statistically significant relationship between the odds of a newborn being hypothermic if the mother was hypothermic. As the authors also discuss, any episode of hypothermia, for mother or infant, is clinically significant (Baker & Lawson, 2012) [p77].

It is reported that despite the side effects of hypothermia being clinically significant for both mother and newborn, and the high rates of hypothermia reported, that the use of warming interventions during caesarean section is low. The use of warming interventions in the United States (Carpenter & Baysinger, 2012) and Australia has not been quantified, but a telephone survey of maternity departments in the UK reported its usage to be as low as 16%, (Woolnough, Hemingway, et al., 2009) despite warming interventions being readily available within the institutions included.

Warming interventions can be broadly categorised as either passive or active. Warming can be applied preoperatively, intraoperatively and postoperatively. Multiple studies in different patient populations (including caesarean section patients) suggest that preoperative warming strategies are effective at reducing incidence of inadvertent perioperative hypothermia, (Andrzejowksi, et al., 2008;

Bock, Muller, Bohrer, Martin, & Motsch, 1998; Chung et al., 2012; Just, Trevlen, Delva, & Lienhart, 1993; Munday, Hines, & Chang, 2013) by increasing peripheral heat content and therefore reducing the intraoperative core-periphery heat gradient through which heat loss occurs. Passive warming strategies usually refer to the use of warmed cotton blankets or other covering such as reflective (often called 'space') blankets and these have the benefit of tending to be cheaper per unit, however less effective than other modes of warming. Active warming interventions may include the use of forced-air warming devices, circulating-water garments, intravenous fluid warming and heated mattresses: some of these interventions have been tested for the caesarean section population (Butwick, et al., 2007; Chakladar, et al., 2011; Fallis, et al., 2006; Horn, et al., 2002; Woolnough, Allam, Hemingway, Cox, & Yentis, 2009; Yokoyama et al., 2009).

Primary research investigating IPH prevention and treatment for caesarean section patients has been undertaken and this varies in terms of quality and usefulness. Despite the use of forced air warming being well supported by systematic reviews (Galvao, et al., 2010; Moola & Lockwood, 2011) and by evidence-based guidelines (Hooper, et al., 2010; NCCNSC 2008) for other patient groups (excluding pregnant patients), the use of this intervention for caesarean section patients has been investigated with differing results (Butwick, et al., 2007; Fallis, et al., 2006; Horn, et al., 2002). Two studies investigating forced air warming (one upper body warming and warmed fluids, one lower body warming) found it to have no effectiveness for CS patients (Butwick, et al., 2007; Fallis, et al., 2006), whilst another study utilising upper body warming found that hypothermia and shivering were reduced by use of the intervention (Horn, et al., 2002). Results from Butwick et al.'s study of lower body warming need to be considered with caution, due to confounding introduced by ten out of 15 of the control group also receiving warming (Butwick, et al., 2007). Blinding is not clear, or not addressed in these forced air warming studies (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002), however the difficulties associated with blinding both participants and outcome assessors to an intervention that is often noisy and not easily disguised, are apparent. Objective measurements, such as temperature, may be at less risk of bias from the lack of blinding, however studies of warming often assess subjective data, such as thermal comfort, therefore the risk of bias from inadequate blinding is of greater concern in these instances.

Intravenous fluid warming has also been used for IPH prevention in this population but with conflicting results (Fallis, et al., 2006) utilising both fluid and forced air warming, found no beneficial effect on perioperative hypothermia, but another study found mothers in the intervention group to have higher core temperatures from delivery to the end of surgery (Yokoyama, et al., 2009), although blinding and allocation concealment were not clear in this study. The usefulness of fluid warming may depend on key factors such as the rate, volume and actual infusion temperature achieved and, as such, fluid warming studies present variations in study design related to these factors.

A key differential between the studies described may be the use of intrathecal morphine (Halloran, 2009), which is thought to play a role in the development or prolonging of inadvertent perioperative hypothermia in some patients. In those studies in which patients received intrathecal morphine (Butwick, et al., 2007; Fallis, et al., 2006), warming interventions were not found to be effective (Halloran, 2009) although there may be other methodological and intervention factors which influence these findings, such as operating temperatures of the devices and the ambient temperature of the environment. The use of intrathecal morphine does have side effects, and one such side effect is the development of profound intrathecal morphine related hypothermia.

2.7 PROFOUND INTRATHECAL MORPHINE RELATED HYPOTHERMIA

The use of intrathecal morphine during obstetric neuraxial anaesthesia is commonplace. Local anaesthetics such as bupivacaine are injected into the subarachnoid space to achieve spinal anaesthesia and opioids, such as fentanyl or morphine, are added to enhance analgesia during surgery and prolong postoperative pain relief (Hess, et al., 2005; Hughes, et al., 2002; Ryan, et al., 2012). Common side effects of morphine experienced by patients include pruritus (itching), nausea and vomiting, while respiratory depression is also a risk. Whilst there are high rates of hypothermia during and after spinal anaesthesia amongst women undergoing caesarean section, some women who receive intrathecal morphine develop particularly problematic and prolonged hypothermia (Hess, et al., 2005; Hui et al.,

2006; Kavee, Ramanathan, Bernstein, Zakowski, & 1991; Sayyid, Jabbour, & Baraka, 2003; Wishaw, 1997).

An early report of problematic or prolonged hypothermia, with paradoxical symptoms, associated with intrathecal morphine was published in the form of a case report in 1992 (Kosai, et al., 1992). Since this time, further recognition of the problem has occurred (Bicalho, et al., 2006; Hess, et al., 2005; Hui, et al., 2006; Ryan, et al., 2012; Sayyid, et al., 2003; Wishaw, 1997). Profound intrathecal morphine-related hypothermia is characterised by a prolonged episode of profound temperature drop, which is, in most cases, accompanied by diaphoresis and sometimes nausea, thus causing extreme discomfort for patients in the postoperative phase. Profound hypothermia has been reported at temperatures as low as 33.1°C (Kosai, et al., 1992) and the time taken for the hypothermia to resolve has been reported at between 2hrs (Hess, et al., 2005) to 19hrs (Kosai, et al., 1992).

For caesarean section patients, this can interfere with recovery in the immediate postoperative period (Butwick, et al., 2007; Halloran, 2009), (an important phase during which bonding and breastfeeding are initiated), while resolution of the hypothermia and associated symptoms are sought. It is difficult to treat. Some studies have found conventional warming methods, both passive and active, to have little benefit during prolonged intrathecal morphine related hypothermia (Hess, et al., 2005; Kosai, et al., 1992; Ryan, et al., 2012; Sayyid, et al., 2003) and these may not be tolerable for a patient who feels hot and sweaty, despite their hypothermic temperature.

Our knowledge regarding profound hypothermia and intrathecal morphine tends to be from case reports and anecdotal sources, mainly consisting of published correspondence. There is however one observational study that has reported on the incidence of intrathecal morphine related hypothermia after caesarean section (Hess, et al., 2005), and one controlled trial published in 1991 that found that women undergoing spinal anaesthesia with intrathecal morphine for caesarean section had significantly lower temperatures for up to 24 hours, as compared to those who received epidural morphine (Kavee, et al., 1991).

The exact mechanism by which intrathecal morphine contributes to hypothermia is not yet known (Butwick, et al., 2007). It is thought that cephalic spread of the morphine contributes to hypothermia in patients given intrathecal morphine (Hess, et

al., 2005) who develop prolonged hypothermia. It has been suggested that morphine spreads in the cerebrospinal fluid (CSF) to the hypothalamus and thus acts on the temperature set point (Hess, et al., 2005). The possibility of morphine dosage amounts being related to the likelihood of profound hypothermia developing has been considered however, even relatively small doses of morphine (150mcg) have been shown to promote a hypothermic effect (Hui, et al., 2006). A recent randomised study compared the hypothermic and pain-relieving effect of a very small dose (50mcg) and a dose of 100mcg of intrathecal morphine (Ischak et al., 2013). This study found no statistically significant difference in body temperature or postoperative pain, or time to nadir temperature between groups. However, the lowest temperature recorded in this study was 34.9°C, and it is not reported in which group of participants this was recorded (Ischak, et al., 2013), thereby limiting the usefulness of the results.

In other populations, the height of spinal blockade and increasing age have been identified as predictors of hypothermia after spinal anaesthesia without intrathecal morphine (Frank, et al., 2000). Central regulatory control under spinal block was also studied in men undergoing urology surgery. More extensive spinal blocks (higher blockades) resulted in greater thermoregulatory impairment than less extensive blocks (lower blockades) in this population (Frank, et al., 2000). The height of spinal blockade may be a factor worth exploration in the investigation of the mechanism by which intrathecal morphine causes prolonged hypothermia in some women.

Studies with small sample sizes have investigated effective warming methods for women undergoing caesarean section, both under spinal anaesthesia with/without intrathecal morphine and epidural anaesthesia. Preoperative (Horn, et al., 2002) and intraoperative warming has been shown to improve outcomes for newborns as well as mothers, but in studies where mothers have received intrathecal morphine, intraoperative warming has had less effect (Butwick, et al., 2007; Fallis, et al.; Hess, et al., 2005). No prior studies have been conducted, however, utilising preoperative warming strategies in the population of women receiving intrathecal morphine for caesarean section. In addition, active warming methods may not be tolerable for these patients, due to the symptoms of sweating and discomfort described.

There is some evidence that pharmacological treatments can be helpful in the treatment of profound and problematic intrathecal morphine related hypothermia in

the face of more widely used warming techniques failing to be effective or tolerable. Case reports only describe the effectiveness of Lorazepam (a benzodiazepine) in resolving intrathecal morphine induced profound hypothermia (Hess, et al., 2005; Ryan, et al., 2012). Additionally, the use of Naloxone has been described, via case reports only, for the same purpose (Bicalho, et al., 2006; Sayyid, et al., 2003; Wishaw, 1997). Opioids have been given to decrease muscle shivering as they are known to modify the shivering threshold but in the case reports described (Sayyid, et al., 2003) excessive sweating alongside shivering instead is noted (Bicalho, et al., 2006), with shivering and sensation of cold returning after the administration of drugs such as Lorazepam.

2.8 RESEARCH PROBLEM

Identification of optimum warming methods for women undergoing caesarean section is required to enable the implementation of best practice in relation to reducing perioperative hypothermia for this group of patients, for whom guidance is currently lacking. Established warming techniques and regimes in other patient populations may have decreased effectiveness or appropriateness for women undergoing caesarean section. For example, the effectiveness of forced air warming systems may depend on the portion or extent to which the body is covered. It may be that during caesarean section sufficient body coverage required to fully benefit from forced air warming is impossible.

In addition, for the subset of women who develop prolonged hypothermia after receiving intrathecal morphine alternative and specific strategies may be required. To formulate these strategies, an in depth understanding of the incidence, mechanism and factors contribute to prolonged hypothermia following intrathecal morphine administration would be beneficial, as would an exploration of the effectiveness of strategies that are currently used to manage this problem. Determining relevant factors that result in morphine related hypothermia in some patients but not others may assist to develop the best methods of treatment as well as prevention of the problem (which is always preferable). The factors which make some patients receiving intrathecal morphine more susceptible than others to develop profound morphine related hypothermia, are not well understood. It is also not known whether

methods of administration or spinal technique related factors affect the likelihood of the condition developing. Treatment regimes, both from a medical or nursing standpoint, would be useful in the management and prevention of both profound intrathecal morphine related hypothermia and the more commonplace inadvertent perioperative hypothermia that occurs after caesarean section surgery. It is not yet known whether preoperative warming would benefit the population of women receiving intrathecal morphine for caesarean section.

2.9 SUMMARY

Inadvertent perioperative hypothermia in women undergoing neuraxial anaesthesia for caesarean section is a significant clinical issue and there is a lack of guidance to assist health care practitioners to prevent or treat this condition. Practical considerations specific to the obstetric population may limit the usefulness of warming interventions currently used for the general surgical population. In addition, a subset of women may develop profound and prolonged hypothermia after neuraxial anaesthesia for caesarean section: this is thought to be related to the use of intrathecal morphine for prolonged analgesia. Limited research has been conducted on this topic and the existing evidence mainly comprises of case reports. Even for those women not experiencing profound and prolonged hypothermia, intraoperative warming appears to have been less effective in the population of women receiving intrathecal morphine, however the use of preoperative warming, particularly in relation to timing and duration, has not yet been tested. Thus, effective treatment and prevention regimes for this population are yet to be confirmed.

Chapter 3: Effectiveness of Warming Interventions on Maternal Core Temperature for Women Undergoing Caesarean Section.

3.1 INTRODUCTION

Given that systematic reviews form the highest level of evidence ((NHMRC 1999) providing a basis for evidence-based health care recommendations (Merlin, Weston, & Tooher, 2009) and that a lack of synthesised evidence was found regarding the management of perioperative hypothermia amongst women undergoing caesarean section, a systematic review was developed to address this deficit. This systematic review was based upon a published protocol (Munday, Hines, & Wallace, 2012), developed by the author, following the methodology of the Joanna Briggs Institute (JBI) for the systematic review of quantitative evidence. The review included 12 studies deemed to be of sufficient quality for inclusion in the review, utilising both meta-analysis and narrative analysis to form recommendations for practice and further research. The full version of the review was published in the JBI Database of Systematic Reviews and Implementations Reports (Munday et al., 2013) and is included in Appendix A. Several publications arose from the full systematic review including a shortened version of the review (Munday et al., 2014), the full published JBI review (Munday et al., 2013), and a JBI Best Practice Information Sheet (Giles et al., 2013). The following publication will be presented in this chapter: Munday J, Hines S, Wallace K, Chang AM, Gibbons K, Yates P. A systematic review of the effectiveness of warming interventions for women undergoing caesarean section. Worldviews on Evidence-Based Nursing. 2014. 11(6): 383-393. (Munday, et al., 2014)

The JBI MAStARI Appraisal Tool for Randomised Controlled Trials, utilised in the review, is included in Appendix B. Also included as appendices are the search strategy (Appendix C), search results (Appendix D), verification of study eligibility form (Appendix E), customised data extraction instrument (Appendix F), included

studies (Appendix G), excluded studies (Appendix H) and the JBI Levels of Evidence (Appendix I).

In addition to the primary outcome of maternal core temperature, the full review (Munday et al., 2013) included the secondary outcomes of maternal shivering, maternal thermal comfort, length of stay in PACU (Post Anaesthetic Care Unit), newborn temperature measured at birth, Apgar scores at 1, 5 and 10 minutes, and newborn umbilical pH. The results for these secondary outcomes will be presented in the following Chapter 4.

3.1.1 Contribution of Authors

The concept for the systematic review was based upon the deficit of synthesised evidence for the prevention of perioperative hypothermia (as established in Chapter 1), and also arose from my previous evidence-based practice project in the area of perioperative hypothermia for the general adult population, as well as my area of practice in the obstetric PACU caring for many women experiencing perioperative hypothermia.

The author team for the systematic review was J Munday, S Hines, K Wallace, K Gibbons and P Yates. I am identified as the principal and corresponding author, based on the criteria specified by the International Committee of Medical Journal Editors (ICMJE 2016), and the primary reviewer for this review (see Appendix J, Statement of Contributions).

3.2 PUBLISHED SYSTEMATIC REVIEW (WORLDVIEWS ON EVIDENCE-BASED NURSING)

Abstract

Background: Women undergoing caesarean section are vulnerable to adverse effects associated with inadvertent perioperative hypothermia, but there has been a lack of synthesized evidence for temperature management in this population. This systematic review aimed to synthesize the best available evidence in relation to preventing hypothermia in mothers undergoing caesarean section surgery.

Methods: Randomised controlled trials meeting the inclusion criteria (adult patients of any ethnic background, with or without co-morbidities, undergoing any mode of anaesthesia for any type of caesarean section) were eligible for consideration. Active or passive warming interventions versus usual care or placebo, aiming to limit or manage core heat loss in women undergoing caesarean section were considered. The primary outcome was maternal core temperature. A comprehensive search, with no language restrictions, was undertaken of multiple databases from their inception until May 2012. Two independent reviewers using the standardized critical appraisal instrument for randomised controlled trials from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instruments (JBI-MASTARI) assessed retrieved papers for methodological quality and conducted data collection. Where possible, results were combined in a fixed effects meta-analysis using the Cochrane Collaboration Review Manager software. Due to heterogeneity for one outcome, random effects meta-analysis was also used.

Results: A combined total of 719 participants from 12 studies were included. Intravenous fluid warming was found to be effective at maintaining maternal temperature and preventing shivering. Warming devices, including forced air warming and under-body carbon polymer mattresses, were effective at preventing hypothermia. However, effectiveness increased if applied preoperatively. Preoperative warming devices reduced shivering and improved neonatal temperatures at birth. Intravenous fluid warming did not improve neonatal temperature and the effectiveness of warming interventions on umbilical pH remains unclear.

Linking Evidence to Action: Intravenous fluid warming by any method improves maternal temperature and reduces shivering during and after caesarean section, as does preoperative body warming. Preoperative warming strategies should be utilized where possible. Preoperative and/or intraoperative warmed IV fluids should be standard practice. Warming strategies are less effective when intrathecal opioids are administered. Further research is needed to investigate interventions in emergency caesarean section surgery. Larger scale studies using standardized, clinically meaningful temperature measurement time points are required.

Introduction

Women undergoing caesarean section are vulnerable to perioperative core temperature decline in part due to vasodilation and neuraxial anaesthesia (Dunn, York, Cheek, & Yeboah, 1993). Inadvertent perioperative hypothermia (IPH), defined as a core temperature below 36°C related to undergoing surgery (NCCNSC, 2008) is a common, but detrimental, condition with serious adverse effects, affecting both mothers and neonates. Babies born to hypothermic mothers may be at risk of lower temperatures, umbilical pH and Apgar scores at birth (Petsas, Vollmer, & Barnes, 2009, Horn et al., 2002). In addition, IPH has potential to adversely affect maternal experiences due to discomfort and disruption from shivering, which can impair the mother's ability to initiate breastfeeding.

Earlier systematic reviews (Galvao, Liang, & Clark, 2010; Moola & Lockwood, 2011) and guidelines for IPH management (AORN, 2007; ASPAN, 2001; Hooper et al., 2010; NCCNSC, 2008) focus on adults or all age populations, and have excluded pregnant or caesarean section patients. Evidence-based IPH guidelines are required for this population as not all established recommendations targeting the general population are transferable to caesarean section patients (Chakladar & Harper, 2010). Practical problems may exist with forced air warming (recommended by NICE (NCCNSC 2008)) for obstetric patients (Chakladar, Dixon, & Harper, 2011; Chakladar & Harper, 2010; Petsas et al., 2009). Any risks associated with warming may be magnified for pregnant patients as maternal overheating or high maternal body temperature may also adversely affect fetal wellbeing (Lieberman et al., 2000).

In addition, thermoregulatory responses of pregnant women may influence the effectiveness and appropriateness of warming; for example, vasodilation is exacerbated by neuraxial anaesthesia and oxytocics, thus heat loss is increased (Liu & Luxton, 1991). If not managed, the rate of hypothermia in patients undergoing spinal anaesthesia for caesarean section could be as high as 80% (Harper & Alexander, 2006). However, hypothermia is usually initially undetected during neuraxial anaesthesia due to a lack of temperature monitoring (Arkiliç, Akça, Taguchi, Sessler, & Kurz, 2000; Sessler, 1997) and behavioural thermoregulation impairment (Arkiliç et al., 2000). Even in small amounts, intrathecal morphine is known to be associated with hypothermia (Hui et al., 2006). Cephalic spread of intrathecal morphine is proposed to decrease the thermoregulatory set point (Hess,

Snowman, & Wang, 2005) which may explain the paradoxical symptoms sometimes found with intrathecal morphine- associated hypothermia, whereby diaphoresis alongside hypothermia has been observed (Hess et al., 2005). As active warming may not be tolerable for these patients, thermal maintenance in patients given intrathecal morphine presents a greater challenge.

This review seeks to synthesize the best available evidence, and to address the lack of existing guidance, for the outcome of hypothermia prevention in mothers undergoing caesarean section by providing recommendations specifically for this population. Differences in effectiveness for warming interventions between different modes of anaesthesia for caesarean section are also examined. This article is derived from a published systematic review (Munday, et al. 2013) which also included further outcomes relating to maternal shivering, thermal comfort, neonatal temperature at birth, Apgar scores and umbilical pH, which was developed from a published systematic review protocol (Munday, Hines, & Wallace, 2012).

Objectives The main objective of this review was to synthesize the best available evidence on the effectiveness to prevent hypothermia in women undergoing caesarean section. The review also asked whether there were any differences in effectiveness between patients undergoing different modes of anaesthesia for caesarean section.

Methods

Inclusion criteria

Participants The review included adults over the age of 18 years, of any ethnic background, with any co-morbidities, undergoing either elective or emergency caesarean section under any mode of anaesthesia (spinal, epidural, combined spinal-epidural or general anaesthesia), receiving interventions to prevent or treat heat loss.

Interventions This review included active or passive warming interventions versus usual care or placebo applied to women undergoing caesarean section surgery, applied either preoperatively or intraoperatively. Active warming interventions include forced air warming devices, warmed intravenous fluids, warmed mattresses

and warmed coverings. Passive warming interventions include unheated coverings, such as leg wrapping.

Outcomes

Primary outcome. Maternal core temperature, measured during the preoperative, intraoperative and postoperative phases.

Secondary outcomes. Maternal shivering, maternal thermal comfort, length of stay in PACU (Post Anaesthetic Care Unit), newborn temperature measured at birth, Apgar scores at 1, 5 and 10 minutes, and newborn umbilical pH (results for secondary outcomes available in the full published version of this review; Munday et al. 2013).

Study Design Any randomised controlled study that met the inclusion criteria with reduction of perioperative hypothermia as a primary or secondary outcome was considered.

Search Strategy The electronic search sought published, unpublished and grey literature, in any language in CINAHL, Embase, ProQuest, Web of Science, Scopus, Current Contents, CENTRAL, Dissertation and Theses PQDT (via ProQuest), Mednar, Open Grey and Clinical Trials, from the inception of the databases until May 2012. The full search strategy is available within the full published systematic review (Munday, et al. 2013). Initial keywords included: perioperative or preoperative or intraoperative, surgical, temperature or core temperature, thermoregulation, hypothermia, shivering, Caesarean section, Caesarean delivery, parturient, maternal, warming, active warming, passive warming.

Review methods. The full article was retrieved for all those search results that appeared to meet the inclusion criteria, and were assessed for relevance to the review using a form developed by the reviewers and based on the recommendations of the Cochrane Collaboration (Higgins & Deeks, 2011). Two independent reviewers assessed methodological quality of papers using the standardized critical appraisal instrument for RCTs from JBI-MASTARI (see Appendix I and II). Disagreements regarding three papers were adjudicated by consultation with the third reviewer.

Two independent reviewers extracted data using the previously piloted data extraction tool, based on the JBI data extraction tool for quantitative studies. Additional information was requested from authors of five included studies (Chakladar, Dixon, & Harper, 2012; Chung et al., 2012; Fallis, Hamelin, Symonds, & Wang, 2006; Reidy, Preston, Douglas, Sherlock, & Tyler, 2008; Woolnough, Allam, Hemingway, Cox, & Yentis, 2008), three of whom provided additional information (Chakladar et al., 2012; Fallis et al., 2006; Reidy et al., 2008).

Where meta-analysis was possible, results were combined in a fixed effects meta-analysis using the Cochrane Collaboration Review Manager software (RevMan 5.2; The Nordic Cochrane Centre, Copenhagen, Denmark). Due to heterogeneity for one comparison and outcome, random effects meta-analysis was also used. Results of the meta-analysis are presented using odds ratio (OR; for categorical data) and weighted mean difference (for continuous data), along with their 95% confidence intervals (CI). Heterogeneity was assessed using the standard Chi-square test and I2. Standard deviation (SD) was calculated from the standard error of the mean (SEM; Rosner, 2011; The Joanna Briggs Institute, 2008) reported for one study (Smith et al., 2000). Variations between studies, particularly the time points of temperature measurements, meant that only limited meta-analyses were possible. The remaining data were synthesized into a narrative summary.

Results

A combined total of 719 participants from 12 randomised controlled trials (RCTs) were included (Figure 1). Mode of anaesthesia was spinal or epidural anaesthesia in the majority of studies. Maternal core temperature measurement method varied widely but although there are reliability issues between sites the choice of site was not used as a basis for exclusion.

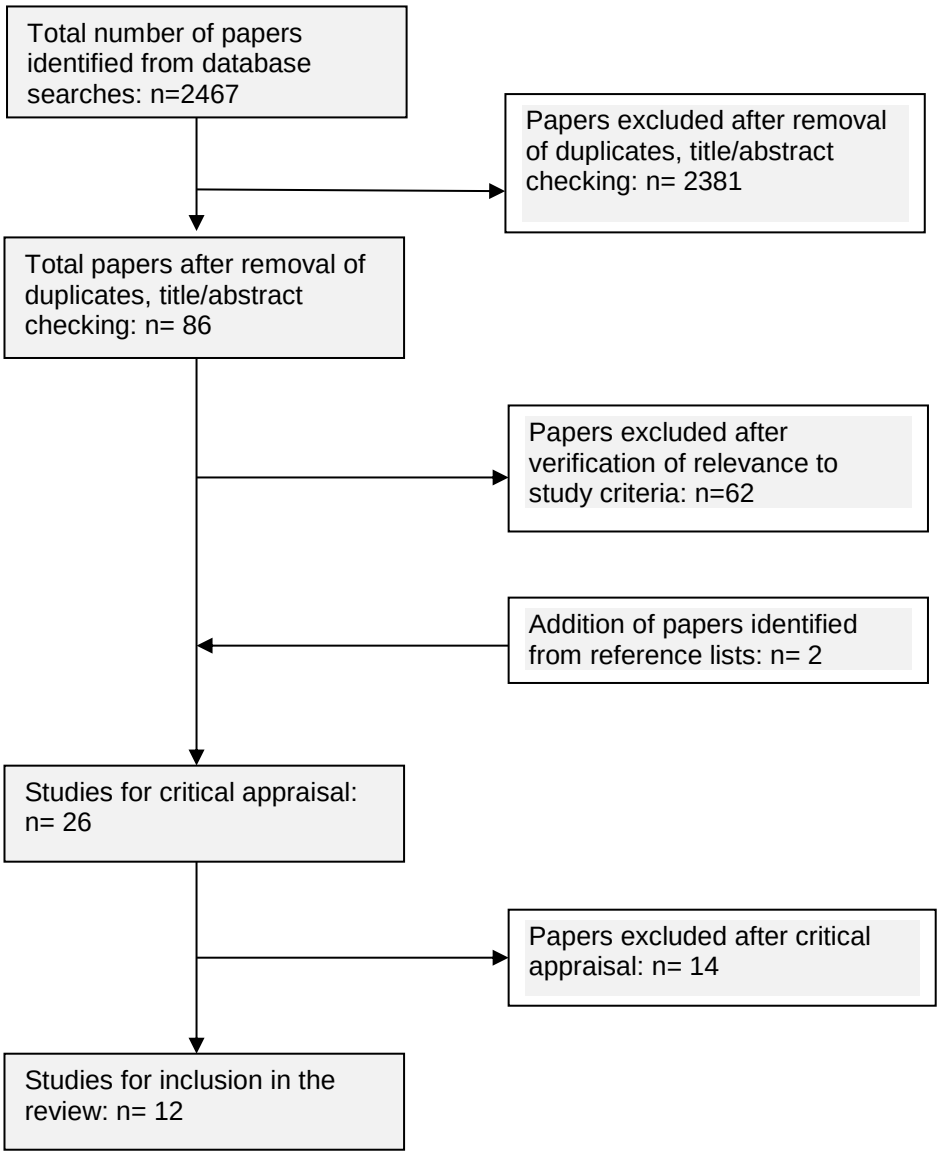

Figure 1: Flowchart of study retrieval and selection

Warmed versus unwarmed IV fluids

Seven studies (Chan, Morley-Forster, & Vosu, 1989; Chung et al., 2012; Goyal Kundra, S., Grewal, A., Kaul, T.K., Singh, M.R., 2011; Oshvandi et al., 2011; Smith et al 2000; Woolnough et al., 2008; Yokoyama et al., 2009) compared intravenous fluid (IV) warming with other interventions, with most using room temperature fluids as a comparator (Chan et al., 1989; Goyal et al., 2011; Oshvandi et al., 2011; Smith et al., 2000; Yokoyama et al., 2009). Wide variation exists in methods of both fluid warming and administration temperatures. Warming cupboards were used in four studies, (Chan et al., 1989; Chung et al., 2012; Woolnough et al., 2008; Yokoyama et al., 2009) with temperature settings ranging between 38-45°C. Two studies (Chung et al., 2012; Woolnough et al., 2008) measured the administration temperature of the fluids at the distal end, and found this to be 37-38°C. The fluid warmers used in three studies were Hotline™ (Smith et al., 2000; Woolnough et al., 2008) and Astotherm™ (Goyal et al., 2011). Fluids in these studies were warmed to 42°C (Smith et al., 2000; Woolnough et al., 2008) and 39°C (Goyal et al., 2011). Water baths were also utilized in two studies (Oshvandi et al., 2011; Yokoyama et al., 2009) as a secondary method of warming the IV tubing to maintain the temperature of the fluids already warmed in a warming cupboard (Yokoyama et al., 2009). The commonly used comparator was 'room temperature' fluids which typically ranged from 20-25°C (Chan et al., 1989; Goyal et al., 2011; Oshvandi et al., 2011; Smith et al., 2000; Yokoyama et al., 2009).

Two studies of IV fluid warming were combined using meta-analysis for mean maternal temperature on arrival to PACU (Figure 2) (Goyal et al., 2011; Smith et al., 2000). The two combined studies compared the temperature on arrival to PACU for women receiving intravenous fluids at room temperature (22°C and 20-22°C) (Goyal et al., 2011:Smith et al., 2000) versus women receiving intravenous fluids warmed via a fluid warmer to either 39°C (Goyal et al., 2011) or via Hotline™ to 42°C (Smith et al., 2000). The administration of warmed IV fluids compared to room temperature fluids at 20-22°C resulted in a significantly higher mean temperature on arrival to PACU (mean difference 0.30, 95% CI 0.11-0.49).

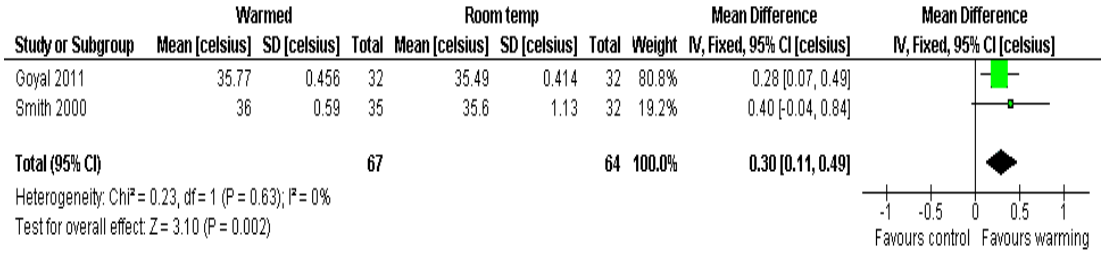

Figure 2: Intravenous fluid warming versus room temperature fluids and mean maternal temperature on arrival to PACU

IV fluid warming was also effective for the outcome of mean maternal temperature after 30 minutes in PACU (Figure 3), showing the higher mean temperature persisted into the recovery phase (mean difference 0.51, 95% CI 0.35-0.68) (Goyal et al., 2011; Smith et al., 2000).

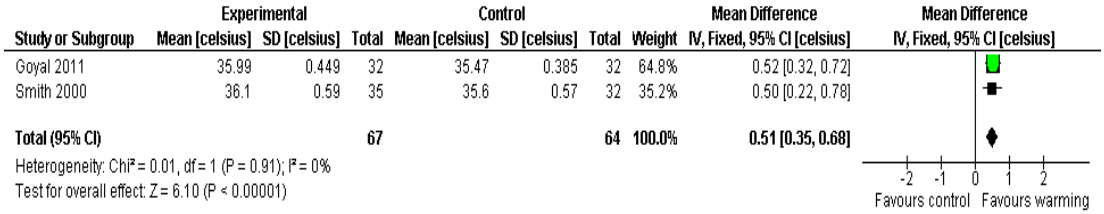

Figure 3: Intravenous fluid warming versus room temperature fluids and mean maternal temperature at 30 minutes in PACU

Smith et al. (2000) also demonstrated a significantly higher maternal temperature at discharge from recovery in the warmed IV fluid group (36.5°C, SD: +/- 0.6°C versus 36.1°C, SD: +/- 0.6°C, p <0.05), but the lack of discharge temperature time points in other fluid warming studies limits comparability.

Warmed IV fluids and reflective blanket resulted in higher tympanic maternal temperature (via thermocouple) at the time of delivery (36.7°C, SD: +/- 0.3°C) versus unwarmed IV fluids and reflective blanket (36.2°C, SD +/- 0.3°C), p <0.05 and repeated measures analysis of variance indicated this higher temperature remained at 15 minutes, 30 minutes and 45 minutes after delivery (36.4° C, SD +/- 0.2°C) versus (35.5°C, SD +/- 0.3°C, p<0.05) (Yokoyama et al., 2009). Another study (Oshvandi et al., 2011) found the average core temperature at the end of anaesthesia was also higher in patients administered pre-surgery warmed IV fluids versus room temperature fluids (36°C, SD: +/- 0.5°C versus 35.34°C, SD: +/- 0.06°C, p<0.05).

A comparison of warmed IV fluids via Hotline™ versus room temperature fluids at multiple temperature measurement time points found a significantly greater number of hypothermic (<36°C) patients at the end of surgery for the unwarmed group (24/32 patients or 75%) versus 16/32 patients (46%) in the warmed group, $p < 0.05$ (Smith et al., 2000). In addition, a significantly lower core final temperature for the unwarmed (control) group (35.6 °C, SD: +/- 0.7°C versus 36.1°C, SD: +/- 0.6°C in the warmed group, $p < 0.05$) was also found.

Patients receiving warmed IV fluids plus warmed skin preparation fluids and extra clothing versus those receiving room temperature fluids had significantly higher mean aural and bladder temperatures between baseline to PACU arrival ($p<0.05$; Chan et al., 1989). There was a 1.0°C (SD: +/- 0.02°C) drop in mean bladder temperature between baseline and arrival in PACU for the control group versus a drop of 0.6°C in the intervention group (SD +/- 0.01°C) ($p<0.05$). Aural temperature decline from baseline to PACU arrival was 0.9°C (SD +/- 0.06°C) in the control group versus 0.5°C (SD +/- 0.04°C) in the intervention group ($p<0.05$).

Aural temperature was significantly higher at 60 minutes after induction of anaesthesia or in the recovery phase in three studies (Chung et al., 2012; Oshvandi et al., 2011; Woolnough et al., 2009) for those who received warmed fluid preload versus room temperature fluids. Although a statistically significantly higher mean aural temperature was found in women receiving warmed intravenous fluid preload (35.9°C SD +/- 0.5°C) compared to those receiving room temperature fluid preload (35.4°C SD +/- 0.6°C, $p=0.001$) in one study, both results are below the cut-off for hypothermia thereby reducing clinical significance (Oshvandi et al., 2011). Similarly, another study of warmed fluid preload versus room temperature preload versus forced air warming (Chung et al., 2012) found that the greatest temperature decrease during the 60 minutes after CSE insertion was by the room temperature group (0.4°C difference, 95% CI 0.2-0.6°C, $p=0.015$).

Finally, a three group study comparing warmed IV fluids via Hotline™ versus cabinet warmed IV fluids versus room temperature fluids found a significantly greater mean infrared aural temperature decrease in the room temperature group during the first 60 minutes following CSE, although the authors only report results for the decrease in room temperature fluids (0.4°C (95% CI 0.2-0.6°C, $p=0.015$) (Woolnough et al., 2008). Warmed IV fluids administered both pre surgery and

during surgery appear to have benefits for increasing maternal temperature, as measured in the latter intraoperative phase and into the recovery phase until discharge.

Warming Devices

Five studies of warming devices were included (Table 1). Data are largely presented by narrative analysis due to clinical heterogeneity (see Table 1). Three forced air warming studies used a 43°C setting for participants (Chung et al., 2012; Fallis et al., 2006; Horn et al., 2002) however in one of these studies (Fallis et al., 2006) heat settings were changed for some participants (one participant commenced on the lower setting of 38°C before progressing to the high setting, while 14 of 32 participants commenced on the higher setting before subsequently adjusting to a lower setting).

Table 1 Forced air warming studies: intervention and comparison groups

Study	**Intervention/s**		**Control**		**Control 2**	
	Forced air warming	**Warmed IV fluids**	**Covering / blanket**	**Warmed IV fluids**	**Covering / blanket**	**Warmed IV fluids**
Fallis et al., 2006	Upper body forced air warming	Yes	Warmed cotton blanket	Yes	n/a	n/a
Horn et al., 2002	Upper body forced air warming	Yes	Single cotton blanket	Yes	n/a	n/a
Chung et al., 2012	Upper body forced air warming	No	Forced air warming blanket switched OFF	Yes	Forced air warming blanket switched OFF	No
Chakladar et al., 2011	Under body carbon polymer warming switched ON	Yes	Carbon polymer warming blanket switched OFF	Yes	n/a	n/a
Reidy et al., 2008	Under body forced air warming	Yes	'standard care' warmed cotton blankets	Yes	n/a	n/a

Chakladar et al.'s unpublished study (Chakladar et al., 2012) of a carbon polymer mattress turned on to 40°C versus a carbon polymer warming mattress turned off (and warmed IV fluids to 41°C in both groups) found a significantly lower incidence of IPH, both statistically and clinically, in the intervention group (3/58 participants) versus the control group (11/58 participants, p = 0.043), but the statistical test was not specified.

Reidy et al.'s (2008) unpublished study of a forced air warming mattress versus 'standard care' found a significant difference between groups in mean maternal temperature on entering PACU: 36.1°C (SD +/- 0.4°C) in the intervention group versus 35.7°C (SD +/- 0.5°C) in the control group (p=0.01). The mean difference for the two studies, when combined using random effects meta-analysis, favours under body warming in comparison to warmed cotton blankets or warmed IV fluids alone, for initial admission temperature to PACU (0.29, 95%CI 0.09 to 0.48; see Figure 4).

Moderate heterogeneity (Deeks, Higgins, Altman, 2011) as indicated by the I^2 value (Figure 4) is noted and there are some differences in the interventions. Both studies utilized under-body warming. However, a carbon polymer mattress at 40°C was used by Chakladar and colleagues (2012), whereas a forced air mattress at 38°C was used by Reidy et al (2008). Control participants in one study received the under-body mattress turned off and warmed IV fluids (Chakladar et al., 2012), whereas the control group in the other study received two warmed cotton blankets plus warmed IV fluids (Reidy et al. 2008). Chakladar et al. (2012) used temporal artery measurements to assess maternal temperature, whereas Reidy et al. (2008) used oral thermometers.

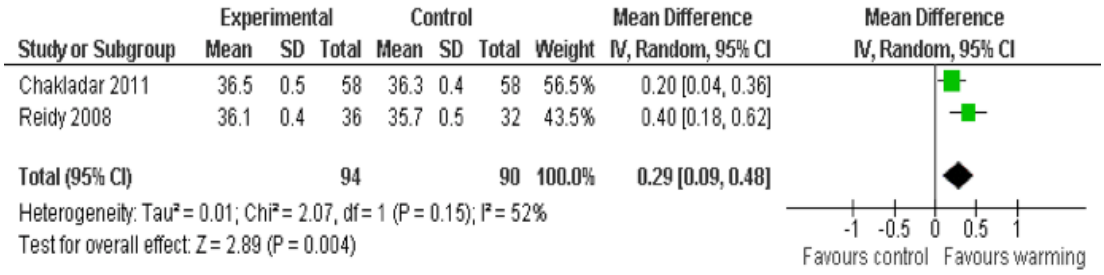

Figure 4 Under body warming mattress versus control and temperature (°C) on PACU arrival.

Chung et al. (2012) reported statistically significant differences (p=0.004) between 'core' temperature decreases (as measured by aural infrared thermometry) at 45 minutes, reporting less temperature decrease in patients in the warmed IV fluid (-0.5°C SD: +/- 0.3°C) and forced air prewarming groups (-0.6°C SD: +/- 0.4°C) than in the control group: (–0.9°C SD: +/- 0.4°C), although the statistical test is not specified.

Table 2 Upper body forced air warming, final maternal OT temperature and variations between studies.

Study	**Ambient OT temp* (°C)**		**Anaesthetic Mode**	**Opioid**	**Warming (timing)**	**Final maternal temperature in OT * (°C)**		
	Interventi-on	**Control**				**Interve-ntion**	**Control**	***P* value**
Fallis et al., 2006	Entrance: 21.6 ± 1.2. Exit: 23 ± 1.2.	Entrance: 21.6 ± 0.9 Exit: 22.2 ±0.6	Spinal	Intrathecal morphine Fentanyl citrate	Intraopera-tive	36.1°C± 0.4°C	35.9°C ± 0.4°C	NS (via independent t test)
Horn et al., 2002	23.9± 0.5	24.1 ± 0.3	Epidural	Nil	Preoperati-ve and intraopera-tive	37.1°C ± SD 0.4°C	36.0°C ± 0.5°C	<0.05 (via Student's *t* test)

* mean and SD

Fallis et al.'s (2006) study of intraoperative upper body forced air warming also reported mean oral temperature decrease during the procedure up to 60 minutes (thereafter data was omitted due to decreased sample size). Mean temperature decrease was not statistically or clinically significant: -0.8°C SD: +/- 0.5°C (control group) versus -0.7°C SD: +/-0.4°C (intervention group) via repeated measures ANOVA (p=0.508). Differences in the mean final temperature on exit from the operating theatre were also not statistically significant (35.9°C SD: +/- 0.4°C in the control group versus 36.1°C SD: +/- 0.4°C in the intervention group, p=. 189).

In contrast to Fallis et al.'s (2006) study, significantly (p<0.001) higher operating room final temperatures were found in patients in Horn et al.'s (2002) prewarming study for the forced air warming group where participants received 15 minutes of forced air prewarming plus intraoperative warming (37.1°C SD: +/- 0.4°C) versus (36.1°C SD +/- 0.5°C) in the control group.

These results suggest that forced air preoperative warming plus intraoperative warming is more effective at maintaining maternal intraoperative temperature than

intraoperative forced air warming alone. The strongest results for forced air warming for maternal temperature maintenance during caesarean section thus far have been achieved from preoperative application. Although under body warming mattresses achieved higher maternal core temperatures in comparison with warmed cotton blankets, there were few studies examining this intervention.

One study (Sun et al., 2004) compared tight versus loose elastic bandage leg wrapping in women undergoing elective caesarean section under epidural anaesthesia, where reduction of hypothermia was a secondary outcome. Maternal sublingual temperature was recorded every three minutes35 at five 'observation times', however only baseline and delivery results were reported, with no significant differences and no p values reported (tightly wrapped group 36.5°C, SD: +/- 0.4°C at delivery versus the loosely wrapped group 36.4°C, SD: +/- 0.3°C), with the average reduction from baseline to delivery also given: tightly wrapped group (0.4°C, SD: 0.2°C) versus loosely wrapped group (0.5°C, SD: 0.3°C). From this single study, leg wrapping presented no benefits for maintaining maternal temperature, however, these observations should be considered with caution as they are only derived from a single study.

Conclusions

This review includes 12 RCTs in three broad categories of interventions within the specific population of women undergoing caesarean section. Methodological issues, variations in outcome measurement methods, insufficient homogeneity of control groups between the studies and in some cases limited extractable data reduced synthesis by meta-analysis and thus the strength of recommendations made by this review. Wide but subtle variations in treatments also impacted on homogeneity. Although there are questions about the reliability and accuracy of the wide range of temperature measurement devices and routes used across all included studies, this was beyond the scope of this review. Consistency of the core temperature measurement route within studies was considered as vital, and an indicator of the quality of outcome measurements.

Variations in hypothermia definition were evident despite increasing guidance that core temperatures below 36°C should be considered as hypothermic in perioperative

patients (ASPAN, 2001; Hooper et al., 2010; NCCNSC, 2008). In this review, these variations did not cause difficulties as studies tended to report temperature decline. As the <36°C indicator for hypothermia becomes more widely accepted and incorporated into practice guidelines, its usefulness in clinical studies will increase.

As there were too few included studies that utilized different modes of anaesthesia, no assessment of effectiveness of interventions in relation to anaesthesia mode was possible. However, forced air warming was less effective where participants received intrathecal morphine (Fallis et al., 2006; see Table 2). Addition of intrathecal opioids, in particular morphine, may have influenced the degree and incidence of hypothermia and therefore the effectiveness of interventions included in this review. The use of opioids is not clear in all studies, therefore limiting the analysis of this issue.

Findings that warmed IV fluids are effective in maintaining normothermia are consistent with an earlier systematic review of a broad population (Moola & Lockwood, 2011), and support NICE guidance (NCCNSC, 2008) that has so far applied to only non-pregnant patients. NICE guidelines support the warming of fluids to 37°C for volumes of 500mls and above (NCCNSC, 2008). All but one (Chan et al., 1989) of the included fluid warming studies in this review warmed fluids to 37°C or above. When fluids were warmed to a lower temperature of 36.5°C (Chan et al., 1989) a reduction in heat loss in the warmed group was still found. This review does not make a recommendation of one method of warming fluids over another. Warmed IV fluids should be standard practice for maintaining normothermia for patients undergoing caesarean section, as they are easy to administer and do not appear to cause practical concerns for patients and caregivers.

The effectiveness of preoperative warming strategies in this population is confirmed by this review. Again, this recommendation had previously been provided for either general population groups (Moola & Lockwood, 2011) or non-pregnant patients (NCCNSC, 2008). Preoperative warming provides clinical value in reducing intraoperative heat loss even if used for relatively short periods and may be cost-effective, especially if utilizing existing resources. Horn et al (Horn et al., 2002) emphasize that warming prior to epidural insertion precedes the vasodilation that contributes to hypothermia. The overall effectiveness of intraoperative, as opposed to preoperative, upper body forced air warming is less clear. Horn et al. (2002) found a

combination of both preoperative and intraoperative warming to be effective, however Fallis et al. (2006) found that intraoperative warming alone did not maintain normothermia, although the potential influence of intrathecal opioids administered in this study should be considered. Table 2 also details differences in mode of anaesthesia and ambient temperature between studies.

Concerns regarding practicality and tolerability in pregnant patients were not widespread within these studies. The inability to tolerate active warming were found by participants in one upper-body warming study, (Fallis et al., 2006) during which some participants adjusted to a lower setting (and one participant commenced on a low setting before increasing). Forced air warmers are generally designed to progress to a lower setting automatically after a certain period if the highest setting is chosen. Therefore, the reduction in the temperature setting in Fallis et al.'s (2006) study does not appear to be extraordinary. Fallis et al. (2006) also found that thermal comfort was enhanced by active warming. This suggests the request to reduce the device temperature setting by some participants does not signify widespread warming related thermal discomfort.

Clinician concerns that upper body warming blankets present practical difficulties - especially after delivery - were not an issue in the forced air warming studies in this review (Chakladar et al., 2011; Petsas et al., 2009). Practical difficulties regarding intraoperative upper-body forced air warming may be addressed by preoperative application. In addition, active under-body or lower-body warming may assist with these concerns. Unfortunately no lower body warming studies were of sufficient quality for inclusion. Tolerability of under-body warming in terms of discontinuation of warming via carbon polymer mattress was required for one participant out of 58 who found the intervention too hot (Chakladar et al., 2012). Further study of the effectiveness of carbon polymer mattresses would be beneficial, particularly in comparison to forced air warming mattresses, and also in emergency caesarean section situations where it is suggested that they may make clinical differences, reducing preparation time (Chakladar et al., 2012).

Limitations

Limitations of this review include a predominance of studies of elective patients, therefore limiting applicability to the emergency caesarean section population, which may have resulted in introducing a risk of bias into the review. Also studies were mainly small scale. Meta-analysis was limited due to the clinical heterogeneity of the included studies. Analysis of intraoperative temperature was reduced due to the many variations in temperature reporting points and temperature measurement methods.

Industry sponsorship in the form of equipment donations for 3 of the 12 included studies (Fallis et al., 2006, Horn et al. 2002, Woolnough et al., 2009) could be seen as a limitation to the overall results of this review, however none of these studies contributed to meta-analyses for the outcome of maternal warming.

Linking Evidence to Action

- Preoperative warming interventions lead to improved maternal thermoregulation in caesarean section surgery and should be used whenever possible.
- Intravenous fluid warming increased intraoperative and postoperative temperatures, whether given as a preload or intraoperatively.
- Upper-body forced air warming applied preoperatively achieved better temperature maintenance than if only applied intraoperatively.
- Warming appears to have less effect when intrathecal opioids are administered, however, further investigation into this factor is required.
- Findings from this review, in relation to IV fluid warming and preoperative forced air warming, confirm that recommendations made for general adult groups may be applied to the population of women undergoing caesarean section surgery under neuraxial anaesthesia.

Implications for research

Future studies should be directed to use standardized and clinically meaningful temperature measurement time points including primary endpoints, thus facilitating analysis and comparisons of effectiveness of these interventions. Research is needed to investigate the effectiveness of interventions in emergency caesarean section surgery, as well as studies of the efficacy of lower-body in comparison to upper-body warming, and the use of under-body warming mattresses.

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3.3 CHAPTER SUMMARY

This systematic review was undertaken to synthesise the evidence to examine the effectiveness of warming interventions for preventing and managing inadvertent perioperative hypothermia for women undergoing caesarean section, in the absence of evidence-based recommendations specifically for this population. The shortened systematic review was published in Worldviews on Evidence-Based Nursing and this version of the review, (including the objectives, search strategy, findings, results and conclusions related to the primary outcome of maternal temperature), is presented in this chapter (Munday, et al., 2014). The next chapter will present the results and interpretation of the secondary outcomes of the systematic review, which were published in the full version (Munday, Hines, Wallace, et al., 2013). This version of the review was also used as the basis for a JBI Best Practice Implementation Sheet.

Chapter 4: Effectiveness of Warming Interventions on Secondary Maternal and Neonatal Outcomes

4.1 INTRODUCTION

While preventing maternal heat loss is the primary intention of warming regimes, and is the central focus of this research program, there are a number of secondary outcomes of interest that are linked to maternal heat loss, either directly or indirectly. These secondary outcomes can directly impact upon overall maternal postoperative recovery and experience of caesarean section delivery, and potentially the health status of the newborn after delivery. Therefore, a number of relevant secondary outcomes were considered in the systematic review detailed in Chapter 3. These secondary outcomes were as follows: maternal shivering; newborn core temperature at birth obtained immediately after birth; umbilical pH; Apgar scores; length of PACU and maternal thermal comfort (Munday, Hines, Wallace, et al., 2013). The review methods are detailed in Chapter 3 (and in the full JBI version included in Appendix A). In this chapter, I will present the results and discussion pertaining to these secondary outcomes as an excerpt from the full review:

Munday J, Hines S, Wallace K, Chang AM, Gibbons K, Yates P. 2013. The clinical effectiveness of interventions to assist perioperative temperature management for women undergoing caesarean section: a systematic review. JBI Database of Systematic Reviews and Implementation Reports. 11(6), 45-111

4.2 RESULTS

The findings of the full review are presented according to the included interventions, with sub-headings for each outcome (as per the published version).

4.2.1 Intravenous Fluid Warming

Intravenous fluid warming and prevention of shivering

Six of the seven fluid warming studies (Chan, Morley-Forster, & Vosu, 1989; Chung, et al., 2012; Goyal et al., 2011; Oshvandi et al., 2011; Smith et al., 2000; Woolnough, Allam, et al., 2009) also measured participant shivering. In two studies dichotomous data are presented from the assessment of the presence or absence of shivering (Goyal, et al., 2011; Smith, et al., 2000) before and after caesarean section (Goyal, et al., 2011) or in PACU (Smith, et al., 2000). In addition, details of interventions to treat shivering once it occurred were recorded (number and type) (Goyal, et al., 2011; Smith, et al., 2000). Similar four-point scales recording the degree of shivering intensity were used by two studies (Woolnough, Allam, et al., 2009) (Chan, et al., 1989), while a five point scale was used by Oshvandi (Oshvandi, et al., 2011) attributed to Crossley and Mahajan (Crossley & Mahajan, 1994) and a four point scale was used by Chung et al. (Chung, et al., 2012) attributed to Wrench (Wrench, Cavill, Ward, & Crossley, 1997). Three studies using shivering scales also reported on presence and absence of shivering (Chung, et al., 2012; Oshvandi, et al., 2011; Woolnough, Allam, et al., 2009).

The single study that compared an intervention of warmed fluids, warmed skin preparation and additional clothing with another intervention of room temperature fluids, room temperature skin preparation and single hospital gown (Chan, et al., 1989) could not be included in the meta-analysis (because of the extra interventions) and did not find a significant difference in incidence of shivering between groups (11 of 21 patients reported shivering in the intervention group versus 13/19 in control group, no p value reported). Five studies (Chung, et al., 2012; Goyal, et al., 2011; Oshvandi, et al., 2011; Smith, et al., 2000; Woolnough, Allam, et al., 2009) comparing IV fluid warming with room temperature fluids were combined in a meta-analysis of effectiveness warmed IV fluids on the incidence of shivering (Figure 4).

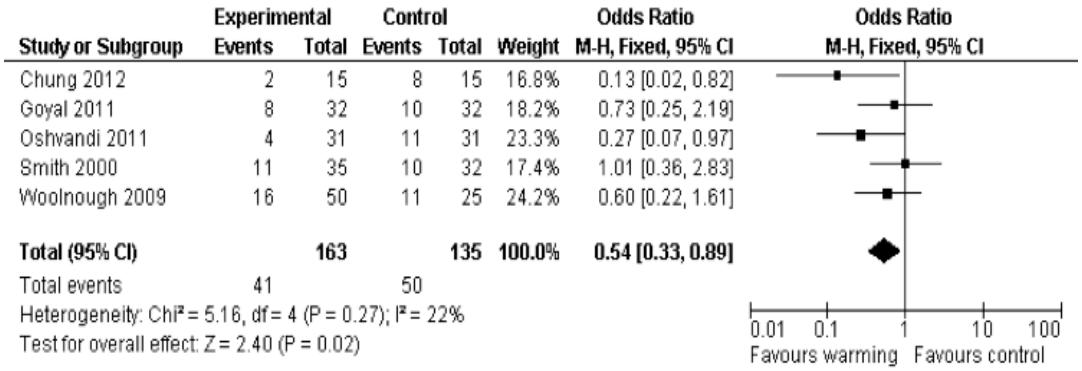

Figure 4: Intravenous fluid warming versus room temperature fluids and the incidence of shivering

Two of the three groups in Oshvandi et al.'s study (Oshvandi, et al., 2011), the warmed IV fluid and room temperature groups, were included in this meta-analysis, as per advice for managing multiple-group studies in the Cochrane Handbook for Systematic Reviews of Interventions (Deeks, Higgins, & Altman, 2011). In addition, for Woolnough et al.'s three group study (Woolnough, Allam, et al., 2009) the two warmed fluid groups were combined together, as the interventions were sufficiently similar, and compared to the room temperature group. The combined result significantly favours intravenous fluid warming (OR 0.54, 95% CI 0.33-0.89) for reducing shivering in this population.

Intravenous fluid warming and maternal thermal comfort

Maternal thermal comfort was assessed by both of the three group studies (Chung, et al., 2012; Woolnough, Allam, et al., 2009). Woolnough et al.'s study of Hotline™ warmed fluids versus warming cabinet fluids versus room temperature fluids used a 0-10 numerical rating scale with 0 indicating 'worst imaginable cold', 5 as 'thermally neutral/comfortable' and 10 indicating 'insufferably hot '(Woolnough, Allam, et al., 2009). The authors considered a score of less than 4 to correspond to feeling cold, whilst a score of more than 6 corresponded to feeling hot. Similarly, Chung et al.'s three group study of warmed IV preload versus unwarmed IV preload (and versus upper body forced air prewarming) which used a 100mm Visual Analogue Scale (VAS) with 0mm indicating 'insufferably hot', 50mm 'thermally neutral' and 100mm as 'worst imaginable cold', reported on thermal discomfort (reporting on data for cold VAS scores between 50mm-100mm) (Chung, et al., 2012).

There was a statistically significant difference in the number of patients reporting thermal discomfort (a thermal comfort score of <4) between the three groups in Woolnough et al.'s three group study (p=0.32) although the statistical test is not specified (Woolnough, Allam, et al., 2009). In the room temperature fluids group: 8/25 (32%) scored <4, whereas 3/25 (12%) scored <4 in the warming cabinet group and only 1/25 (4%) scored <4 in the Hotline group (Woolnough, Allam, et al., 2009). This also appears to be clinically significant: in this study patients demonstrate greater thermal comfort if receiving warmed intravenous fluids. No statistically significant difference or clinically significant (p= 0.093) difference in maternal thermal comfort was found between preload of warmed IV fluid, upper body forced air warming with room temperature preload and room temperature preload (no warming) in Chung et al.'s study with cold VAS data reported (59.3mm, SD: 13.2mm versus 59.0mm, SD: 12.1mm versus 69.0mm, SD: 15.9mm respectively) (Chung, et al., 2012). There were differences between these studies in relation to the temperature settings of fluid warming devices: fluids in Chung's study were warmed to 40°C via a warming cabinet (Chung, et al., 2012), whereas in Woolnough et al.'s study which found a significant difference in thermal comfort from warmed fluids, warming cabinet fluids were stored at 45°C and Hotline™ fluids were set to 42°C (Woolnough, Allam, et al., 2009). Greater volumes of fluid were infused in Woolnough et al.'s study (2.0 litres, SD: 0.4 litres in the room temperature group, 2.1 litres, SD: 0.4 litres in the warming cabinet group and 2.4 litres, SD: 1.4 litres in the Hotline group) (Woolnough, Allam, et al., 2009) as opposed to Chung et al.'s study (1.1 litres, SD: 0.1litres in the room temperature group, 1.2 litres, SD: 0.2 litres in the warmed fluid preload group and 1.2litres, SD: 0.1 litres in the forced air warming group) (Chung, et al., 2012).

These differing results could also be examined in the context of what 'room temperature' refers to in each study. Chung et al.'s study did not report data on ambient temperature (Chung, et al., 2012), whereas Woolnough et al. report that ambient temperature was 24.2°C (SD: +/- 0.9°C) in the room temperature group, 23.9°C (SD: +/-1.4°C) in the warming cabinet group and 24.2 °C (SD: +/-0.8°C) in the Hotline group (Woolnough, Allam, et al., 2009). Woolnough et al. did not examine the differences in ambient temperature between groups in this study

(Woolnough, Allam, et al., 2009). Thus it remains unclear whether differences in ambient temperature explain the conflicting results between these studies.

Intravenous fluid warming and time to discharge from PACU

Time to discharge from PACU was assessed only in two IV fluid warming studies (Goyal, et al., 2011; Smith, et al., 2000) but for one it remains unclear whether time to discharge as reported actually refers to time to fitness for discharge, or actual time to discharge (which may be dependent on many external factors, such as availability of ward staff) (Smith, et al., 2000).

Goyal et al.'s study of warmed IV fluids versus room temperature IV fluids found no statistically significant difference in PACU discharge times in minutes (min) between groups: 105.5min (SD: +/- 9.5min) in the room temperature group versus 107.3min (SD: +/- 9.2min) in the intervention group (Goyal, et al., 2011). Similarly, Smith et al.'s study of warmed IV fluids versus room temperature IV fluids found no significant difference in time to PACU discharge in minutes between groups: 109min (SD: 6min) in the intervention group versus 103min (SD: +/- 7min) in the control group (no p value was reported) (Smith, et al., 2000). The administration of intraoperative warmed IV fluids does not appear to shorten PACU stays for patients.

Intravenous fluid warming and Apgar scores

Apgar scores were evaluated by a paediatrician at one minute after delivery in two IV warming studies, both also using reflective blankets (Chung, et al., 2012; Yokoyama, et al., 2009), but these two studies could not be combined in meta-analysis due to clinical heterogeneity. While study groups were similar in both studies, there were differences between studies in the temperature of warmed fluids, methods of administering warmed fluids and methods of temperature measurement. The Apgar score was significantly higher for the warmed IV fluids group in Yokoyama et al.'s study in comparison to the room temperature fluids group ((Yokoyama, et al., 2009). In Chung et al.'s three group study the Apgar score was lower, but not significantly, for the warmed IV fluid preload compared to the room temperature fluid preload and the upper body forced air warming groups (Chung, et al., 2012) (see Table 1).

Table 1: Apgar scores at one minute – IV fluid warming

Study	Apgar score at one minute			
	Warmed IV fluid*	Room temperature fluids*	Upper body forced air warming	p value
Yokoyama et al (2009)	9 (8-9)	8 (8-9)	n/a	0.029 (Mann-Whitney U-test)
Chung et al (2012) # *preload	8.07 ± 1.10	8.20 ± 0.86	8.13 ± 0.86	0.927* (statistical test not specified)

^ median (range), # mean (SD) * across three groups

No significant difference in Apgar score between groups at five minutes after delivery (p= 0.18) was found by Yokoyama et al (Table 2), in contrast to the statistically significant result for Apgar scores at one minute (Yokoyama, et al., 2009).

Table 2: Apgar scores at five minutes – IV fluid warming versus room temperature fluids (Yokoyama et al, 2009)

Study - Yokoyama et al (2009)	Apgar Score at five minutes (number/total number)		
Apgar score	Warmed IV fluids	Room temperature fluids	p value Mann-Whitney U-test
8	1/15	0/15	0.18
9	12/15	15/15	
10	2/15	0/15	

Intravenous fluid warming and umbilical pH

While umbilical pH was also evaluated in the same two IV fluid warming studies that compared Apgar scores, these studies could not be combined due to clinical heterogeneity because of the source of blood for pH measurement. Chung et al. measured umbilical vein pH immediately after birth (Chung, et al., 2012), whilst Yokoyama et al. measured umbilical artery pH (Yokoyama, et al., 2009). Yokoyama et al. reported a statistically significantly higher pH for the warmed IV fluid group in comparison to the room temperature fluid group but the clinical significance of these results is limited (Yokoyama, et al., 2009), while Chung et al.'s study found no

statistically or clinically significant difference between the three groups receiving warming (Chung, et al., 2012) (Table 3). Yokoyama et al. also reported that umbilical pH data were averaged according to the number of patients receiving ephedrine (five participants in both groups) (Yokoyama, et al., 2009).

Table 3: Umbilical pH – IV fluid warming versus room temperature fluids

Study	Umbilical pH: artery (Yokoyama et al 2009)/ vein (Chung et al 2012)			p value
	Warmed IV fluids*^	Room temperature fluids*^	Upper body forced air warming^	
Yokoyama et al (2009)	7.33 ± 0.045	7.29 ± 0.034	n/a	0.023 (via analysis of covariance)
Chung et al (2012) *preload	7.33 ± 0.06	7.35 ± 0.04	7.32 ± 0.04	0.349 (statistical test not specified)

^ mean ± SD

Intravenous fluid warming and neonatal temperature

Of the fluid warming studies, the only study that measured newborn temperature via the rectal route at five minutes after delivery (and after newborn head wrapping and placement under radiant heater) found no statistically or clinically significant difference (p=0.16 Student's t test) between groups (37.2°C, SD: +/- 0.3°C in the warmed fluid group versus 37.0°C, SD: +/- 0.4°C in the unwarmed fluid group) (Yokoyama, et al., 2009). Again, neonatal temperature data in Yokoyama et al.'s study was averaged according to the number of patients receiving ephedrine (Yokoyama, et al., 2009).

Intravenous fluid warming: summary

Warmed IV fluids are effective at improving maternal temperature whether administered pre or intraoperatively, and are also effective at reducing shivering. It remains unclear whether warmed IV fluids have a positive effect on maternal thermal comfort, umbilical pH or Apgar scores. This intervention was also not found to improve newborn temperature at birth or reduce time to discharge from PACU.

4.2.2 Warming devices: covers and mattresses

Warming devices and prevention of shivering

Three of the five forced air warming studies (see Table 1, Chapter 3) included shivering as a secondary outcome (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002). Dichotomous data are presented in terms of presence or absence of shivering, but two studies (Fallis, et al., 2006; Horn, et al., 2002) also present ordinal data in relation to intensity of shivering (slight, moderate/intensive shivering). These two studies (Fallis, et al., 2006; Horn, et al., 2002) use the same four-point shivering scale (0=no shivering, 1=mild shivering, 2=moderate shivering, 3=severe shivering) as used by Chan et al.'s study (Chan, et al., 1989) of warmed IV fluids effect on temperature and shivering in women undergoing CS. Details of these two studies are presented in Table 2, Chapter 3. Chung et al.'s three-group study (Chung, et al., 2012) uses an alternative four-point scale with different descriptors (referenced to Wrench 1997) (Wrench, et al., 1997) and was not entered into the table due to its three-group design and the different scale used for assessing shivering. Again, clinical heterogeneity prevented meta-analysis of these studies in relation to shivering.

Possible bias resulting from unblinded investigators assessing shivering in two of the studies (Fallis, et al., 2006; Horn, et al., 2002) should be highlighted. Blinding of investigators is unclear in the remaining study (Chung, et al., 2012). Shivering assessment took place both during and after surgery (Chung, et al., 2012) and after every 15-minute temperature measurement (Fallis, et al., 2006; Horn, et al., 2002).

Fallis et al. (Fallis, et al., 2006) and Horn et al. (Horn, et al., 2002) again present differing results in relation to the effectiveness of upper body forced air warming but this time related to the presence of shivering: Fallis et al. report that there was no statistically significant difference between groups (Fallis, et al., 2006), whereas Horn et al found that there was a significantly lower level of shivering presence in the preoperative forced air warming group (Horn, et al., 2002) (Table 4). These results can also be considered in light of the other characteristics of these studies presented in Table 2, Chapter 3 and discussed above.

Table 4: Presence of shivering in preoperative upper body forced air warming studies

Study	Presence of shivering		p value
	Upper body forced air warming	Control	
Fallis et al (2006)	10/32	10/30	$p=0.861^{(Mantel-Haenszel test)}$
Horn et al (2002)	2/15	9/15	$p<0.05^{(Fisher's exact test)}$

Results from Chung et al.'s three group study also support the effectiveness of preoperative forced air warming in reducing shivering to 20% (3/15) but not to the extent of warmed IV fluids in which 13% (2/15) experienced shivering versus 53.3% (8/15) in the room temperature fluid group (p=0.035) (Chung, et al., 2012).

Results from these studies (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002) suggest that forced air warming applied in the preoperative phase of care reduces shivering, but forced air warming applied intraoperatively may have less effect on reducing shivering.

Warming devices and thermal comfort

Maternal thermal comfort was measured by the four forced air warming studies (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002; Reidy, Preston, Douglas, Sherlock, & Tyler, 2008), with continuous data gained from the use of self-reported thermal comfort scales. Descriptors of thermal comfort status were common between three studies (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002): 'worst imaginable cold', 'thermally neutral' and 'insufferably hot'; but again narrative summary only is possible due to clinical heterogeneity in relation to slight variations in intervention and control groups between the studies.

Chung et al. (Chung, et al., 2012) and Horn et al. (Horn, et al., 2002) both used a 100mm Visual Analogue Scale (VAS) but with hot/cold scores reversed between the studies (for example, 0 = cold on Horn's scale, (Horn, et al., 2002) but 0 = hot on Chung's scale) (Chung, et al., 2012). Fallis et al. used a 0-10 scale with the above descriptors, with 0 referring to cold and 10 referring to hot (Fallis, et al., 2006). Thermal comfort scores were assessed at 15-minute intervals throughout surgery in both Horn (Horn, et al., 2002) and Fallis et al.'s (Fallis, et al., 2006) studies but time

points of thermal comfort assessment remain unclear in the remaining two studies (Chung, et al., 2012; Reidy, et al., 2008). Additional information was obtained from Fallis et al. in relation to their thermal comfort data, as no data could be extracted from the figures presented in the original published article (Fallis, et al., 2006).

Reidy et al.'s study of an under-body forced air warming mattress versus 'standard care' used a three point Likert scale (with responses of 'too cold', 'comfortable', 'too hot') and reports that maternal thermal comfort did not increase, although no data is provided for this outcome (Reidy, et al., 2008). Again, the risk of bias arising from the lack of blinding of investigators assessing thermal comfort needs to be recognized, but with consideration of the practical difficulties of blinding both patients and investigators to forced air warming. The other under-body warming mattress study in this review (Chakladar, et al., 2011) did not measure thermal comfort but it is interesting to note that further data obtained from the authors confirm that the intervention was discontinued for one patient in the warming group due to the patient feeling hot.

VAS scores were not statistically or clinically significantly different between groups in Chung et al.'s three group study comparing preoperative upper body forced air warming, warmed IV fluid preload and room temperature fluids: 59.0mm (SD: 12.1mm) in the forced air warming group versus 59.3mm (SD 13.2mm) in the warmed IV fluid preload versus 69.0mm (SD: 15.9mm) in the room temperature fluid group (p=0.927, but statistical test not specified), although the latter group's thermal comfort appeared to be warmer (Chung, et al., 2012).

Horn et al. reports data for thermal comfort after 15 minutes of treatment: 52mm (SD: 9mm) in the control group versus 63mm (SD: 11mm) but reports that there were no statistically significant differences in thermal comfort between the groups at other time points (Horn, et al., 2002).

In contrast, Fallis et al.'s study of intraoperative forced air warming found statistically and clinically significant differences in thermal comfort between the study groups in favour of intraoperative warming at 30, 45, 60 and 75 minutes (although at the 75 minute time interval, subject numbers were greatly reduced in both groups) (Fallis, et al., 2006). No data are provided for the 15 minute interval which would facilitate comparison with Horn's study and vice versa no data for further time intervals were provided by Horn et al. (Horn, et al., 2002). Thermal

comfort scores were consistently lower in the control group in Fallis et al.'s study (Fallis, et al., 2006) (Table 5).

Table 5: Thermal comfort scores: Intraoperative upper body forced air warming (Fallis et al 2006)

Time (mins)	Sample size	Thermal comfort scores (0=cold to 10 =hot)		P value (repeated measures ANOVA)
		Intervention: upper body forced air warming	Control: warmed cotton blanket	
		Mean ± SD	Mean ± SD	
30	62	5.7 ± 0.3	4.8 ± 0.3	0.016
45	52	6.3 ± 0.3	4.84 ± 0.3	<0.001
60	37	5.8± 0.4	4.6 ± 0.3	0.014
75	17	5.5 ± 0.3	4.5 ± 0.3	0.045

The characteristics of both Horn et al (Horn, et al., 2002) and Fallis et al.'s studies (Fallis, et al., 2006) (Table 4) are interesting in the context of these varying results, especially in relation to ambient temperature. Ambient temperature on entrance to the operating theatre was lower in Fallis et al.'s study (Fallis, et al., 2006) – a cooler environment may mean that greater thermal comfort could be gained from the application of a warming device. It is also worth noting that 14 women in Fallis et al.'s study requested that the warming device be lowered to a reduced temperature setting during surgery (Fallis, et al., 2006) suggesting that thermal comfort, in terms of feeling too hot, was not optimal for these women throughout surgery.

Results on the effectiveness of forced air warming on maternal comfort are, therefore, inconclusive with varying results between studies. The relationship between ambient temperature and the possibly linked receptiveness of patients to forced air warming should be considered, as should the possibility of high forced air warming settings being intolerable for some patients.

Warming devices and time to discharge from PACU

Time to discharge from PACU was not an outcome of interest in the included warming mattress and coverings studies.

Warming devices and Apgar scores

Apgar scores measured at one minute were an outcome of interest in four studies (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002; Reidy, et al., 2008). Two

studies measured Apgar scores at five minutes (Chung, et al., 2012; Horn, et al., 2002) and one continued to report at ten minutes (Horn, et al., 2002). A paediatrician determined Apgar scores in both Chung et al.' s (Chung, et al., 2012) and Horn et al.'s (Horn, et al., 2002) studies but it is unclear which healthcare professional measured Apgar scores in the remaining two studies (Fallis, et al., 2006; Reidy, et al., 2008). No significant difference in Apgar scores between groups in any of the above studies was found.

Reidy et al.'s study of maternal under-body forced air warming mattress found no statistically significant effect on Apgar scores at one or five minutes: the median Apgar score at one minute was 9 (range 6-10) in the intervention group versus 9 (range 4-10) for the control group (p=0.12, the statistical test was not specified), and median Apgar score at five minutes was 9 (range 8-10) in the intervention group, and 9 (range 9-10) in the control group (p=0.12, the statistical test was not specified) (Reidy, et al., 2008).

Upper body forced air prewarming versus warmed IV fluid preload versus room temperature preload and no forced air warming, also found no statistical or clinically significant difference in mean Apgar scores at one minute between groups (8.1, SD: +/- 0.8 in the upper body warming group versus 8.1, SD: +/-1.1 in the warmed IV fluid group versus 8.2, SD: +/-0.9 in the room temperature group, p=0.927 via analysis of variance) (Chung, et al., 2012). Intraoperative forced air warming also demonstrated no statistically or clinically significant difference in Apgar scores at one and five minutes: median 8 (range 5-9) for the intervention group, median 8.5 (range 3-9) for the control group at one minute and median 9 (range 8-9) for the intervention group, 9 (8-9) for the control group at five minutes (although no p value is provided and it is not clear what statistical test was used) (Fallis, et al., 2006).

Again, results were similar between groups, and no statistically or clinically significant difference was found in the upper body forced air prewarming study that measured Apgar at one, five and ten minutes: at one minute, 9/15 patients obtained an Apgar of 9 in the warmed group, and 9/15 obtained an Apgar of 9 in the control group (no p values reported) (Horn, et al., 2002). It therefore appears that forced air warming does not appear to either increase or decrease Apgar scores at one or five minutes.

Warming devices and umbilical pH

Umbilical pH was also assessed by the four studies above (in which Apgar score was also assessed). Both Chung et al. (Chung, et al., 2012) and Horn et al. (Horn, et al., 2002) measured umbilical vein pH directly after birth. Fallis et al. (Fallis, et al., 2006) and Reidy et al. (Reidy, et al., 2008) also measured umbilical vein pH but the time at which this occurred was not reported. These studies could not be combined for meta-analysis due to key differences in interventions and controls, thus a narrative analysis is presented. Chung's three group study (with a sample size of 15 participants in each of the three groups) found no significant difference in umbilical vein pH measured directly after birth between the three groups (7.3, SD: +/- 0.04 in the forced air warming group versus 7.3, SD: +/- 0.06 in the warmed IV fluid group versus 7.4, SD: +/-0.04 in the room temperature fluid group, p= 0.35 via analysis of variance) (Chung, et al., 2012).

The remaining three studies are presented in Table 8. As with Chung's study (Chung, et al., 2012), both studies by Fallis (Fallis, et al., 2006) and Reidy (Reidy, et al., 2008) found no benefit from maternal forced air warming in regards to umbilical pH. Horn et al.'s study of upper body prewarming presents contrasting results and found that umbilical vein pH was significantly improved in babies born to mothers in the warmed group (Horn, et al., 2002) (see Table 6), with babies in the control groups having a mean umbilical vein pH of 7.24 (SD ± 0.07) versus a mean umbilical vein pH of 7.32 (SD ±0.07) in the intervention group. Information regarding gestation in weeks is not provided by Horn et al. but participants were 'healthy' and booked for elective surgery (Horn, et al., 2002), suggesting that gestation or maternal medical history may not be relevant in the respect of differences in neonatal outcomes in this study. Both Horn et al. (Horn, et al., 2002) and Chung et al. (Chung, et al., 2012) utilized preoperative warming but with differing results. It remains unclear whether forced air warming, in particular when applied during the preoperative phase of care, improves umbilical pH.

Table 6: Umbilical vein pH and forced air warming

Study	Umbilical vein pH #			P value
	Upper body forced air warming*	Under-body forced air warming mattress	Control	
	Mean ± SD	Mean ± SD	Mean ± SD	
Fallis et al (2006)	7.30 ± 0.0^ (n= 31)	n/a	7.30 ± 0.0^ (n= 28)	Not provided
Horn et al (2002)*	7.32 ± 0.07 (n=15)	n/a	7.24 ± 0.07 (n=15)	<0.05 (one-way analysis of variance)
Reidy et al (2008)	n/a	7.30 ± 0.1 (n=36)	7.30 ± 0.04 (n=32)	0.09 (statistical test not specified)

Mean ± SD; ^ SD 0.0 taken directly from article; *applied preoperatively

Warming devices and neonatal temperature

Three of the forced air warming studies also measured neonatal temperature, either as rectal temperature at delivery (Fallis, et al., 2006; Horn, et al., 2002) or axillary temperature one minute after delivery (Reidy, et al., 2008). In Reidy et al.'s study of the use of forced air warming mattress, neonatal temperature was a primary outcome but the study found no statistically or clinically significant difference in neonatal temperature between the warmed and control groups (Reidy, et al., 2008). Mean neonatal axillary temperature at one minute was 36.8°C (SD: +/- 0.3°C) in the warmed group versus 36.9 °C (SD: +/- 0.3°C) in the control group (p= 0.40). The authors report that temperature was also checked at five and ten minutes after delivery but no data was available for inclusion in this review.

Mean newborn rectal temperature was found to be 37.7°C (SD: +/- 0.4°C) in the warmed group (of 32 participants) in Fallis et al.'s study of upper body forced air warming and 37.5°C (SD: 0.4°C) in the control group (of 29 participants), which was stated to be a non-significant statistical difference although no p-value was reported (Fallis, et al., 2006). Horn's study of upper body forced air prewarming, in contrast, did find a statistically and clinically significant higher newborn rectal temperature for

the warmed air group (37.1°C, SD: +/-0.5°C) versus 36.2°C, SD: +/-0.6°C for the control group, p<0.001) (Horn, et al., 2002).

Forced air intraoperative warming (upper body or under-body) did not therefore significantly improve newborn temperature at birth, but upper body forced air prewarming was found to have a positive effect.

Summary

Forced air warming is effective at improving maternal temperatures, particularly if applied preoperatively. Similarly, preoperative warming was found to have an increase in almost 1°C (0.9°C) in mean neonatal rectal temperature at birth whereas intraoperative warming did not. Under-body warming appears to have a positive effect on maternal temperature. Preoperative forced air warming was also found to reduce shivering. Results were inconclusive on the effects of forced air and under body warming on maternal thermal comfort, Apgar scores and umbilical pH.

4.2.3 Leg Wrapping

One study compared leg wrapping with tight elastic bandages with leg wrapping with loose elastic bandages in women undergoing elective caesarean section surgery under epidural anaesthesia, with 30 participants in each group (Sun et al., 2004). The primary outcome was the effect of the intervention on hypotension (a common occurrence during epidural anaesthesia) but reduction of hypothermia and shivering were secondary outcomes.

Leg wrapping is reported as being applied before administration of the epidural but after the attachment of monitoring, preload of unwarmed fluids and the elevation of the patient's legs to 45° (which seems unlikely given the practicalities of administering the epidural).

Leg wrapping and prevention of shivering

Shivering was measured by an observer, blinded to group assignment, and simply assessed as being either present or absent. There was no difference in the presence of shivering between the groups (21/30 participants shivered in both the tight leg

wrapping and also the loose leg wrapping group, p= 0.61) (Sun, et al., 2004). Data for this outcome, as with hypothermia, was only collected until immediately following delivery. As with maternal temperature, leg wrapping is therefore not effective at preventing shivering in this population, based on evidence from this single study.

Leg wrapping and other outcomes

Thermal comfort, time to discharge from PACU, Apgar score, umbilical pH and neonatal temperature were not included as outcomes of interest in this leg wrapping study (Sun, et al., 2004).

Leg wrapping: summary

Leg wrapping was therefore not effective at improving maternal temperature or shivering; however, these observations are derived from a single study and therefore should be considered with caution.

4.3 DISCUSSION

Shivering is commonly experienced during caesarean section surgery performed under neuraxial anaesthesia. Findings from this review indicate that intravenous fluid warming and preoperative forced air warming have a role to play in shivering prevention. Pharmacological therapies, which may be used for shivering, were beyond the scope of this review. Shivering is a complex multifactorial phenomenon (Chan, et al., 1989) and not purely thermoregulatory in all instances. Possible explanations for shivering have been described: thermoregulatory shivering triggered by core hypothermia (Sessler, 2008), shivering as a response to fever development (Sessler, 2008), shivering due to local anaesthetic injection stimulation of cold receptors (Chan, et al., 1989; Sessler, 2008) and finally, shivering due to tremulous muscular activity that is in fact non-thermoregulatory. Intrathecal drugs may also contribute to the development of shivering (Woolnough, Allam, et al., 2009).

Thermal comfort should also be considered in the context of ambient temperature. Operating theatres are generally cool environments, in accordance with clinical

guidelines to this effect – for example, in Australia, Australian College of Operating Room Nurses (ACORN) standards guide operating room temperatures to be between 20-22°C, although provision is made that in certain circumstances, such as for obstetric patients, variations in ambient temperature may be necessary. (Australian College of Operating Room Nurses 2012.) The American Society of PeriAnesthesia Nurses (ASPAN) clinical practice guidelines for the promotion of normothermia state that ambient operating room temperatures should be between 20-25°C (Hooper, et al., 2010) while NICE guidelines state that ambient temperatures should be over 21°C while patients are exposed, and can be reduced once the active warming commences (NCCNSC 2008). Ambient temperature was generally above 22°C for the majority of studies included in this review. The degree of comfort derived from an active warming intervention may be greater if the commencing ambient temperature is lower, as may be evident in the contrasting results seen between Fallis et al. (Fallis, et al., 2006) and Horn et al.'s studies (Horn, et al., 2002). Participants in Fallis et al.'s study were subject to an initially cooler ambient temperature (Fallis, et al., 2006) in contrast to those in Horn et al.'s study, where the ambient temperature was higher (Horn, et al., 2002). Those in the cooler initial environment had a significant increase in thermal comfort scores (Fallis, et al., 2006) whereas those in the warmer environment did not significantly increase thermal comfort (Horn, et al., 2002). Ambient operating room temperature also increased in the forced air warming group in Fallis et al.'s study, and the authors highlight this as a possible contributing factor to higher thermal comfort scores in this group (Fallis, et al., 2006).

Ambient temperature was insufficiently reported in some studies even though it is also particularly relevant to the administration of room temperature fluids. Unfortunately, one study that used room temperature fluids neglected to provide details of ambient temperature for any of the study groups (Chung, et al., 2012), therefore omitting any indication of the administration temperature of the room temperature fluids. Details of oxytocin administration would also be useful when assessing thermal comfort score results, as Woolnough et al. discuss (Woolnough, Allam, et al., 2009), this drug may alter perceptions of warmth due to its tendency to cause facial flushing.

Visual analogue scales (VAS or numerical rating scales were used to measure thermal comfort but there was a variety of shivering scales used, albeit similar in

nature of descriptors. The assessment of shivering relied largely on the subjective assessment of the (often un-blinded) observers. The reliability of the scales used was not addressed and no scale used appears to have been cross-validated.

Although it is known that the temperature status of both mother and newborn are related, the clinical benefit of warming mothers in relation to newborn outcomes is not clear. Populations studied were similar in terms of gestation, age and excluded conditions. Horn et al.'s study of pre- and intraoperative warming versus unwarmed cotton blankets resulted in the most positive neonatal outcomes in regards to umbilical pH and rectal temperature (Horn, et al., 2002), although reasons for this are unclear. Chung et al. suggest that the short prewarming period of 15 minutes in their study was insufficient to affect neonatal outcomes (Chung, et al., 2012). Some conflicting results were found in relation to neonatal outcomes from IV fluid warming: while one study found IV fluid warming increased both Apgar at one minute and umbilical pH (Yokoyama, et al., 2009) another study did not (Chung, et al., 2012). Only one IV fluid warming study measured rectal temperature at birth, and this study measured temperature after five minutes, during which time the newborn had been placed under a warmer (Yokoyama, et al., 2009). While the disparity in neonatal outcomes between existing studies can be considered in relation to study variations, further studies of key neonatal outcomes and maternal warming are required to make more substantive conclusions about clinical benefits to neonates.

4.4 SUMMARY

While the primary outcomes of maternal perioperative hypothermia and heat loss from a systematic review on warming regimes were presented in Chapter 3, this chapter provided evidence on the effect of maternal warming upon other maternal and neonatal outcomes. Shivering, commonly experienced by women during and after caesarean section, is reduced where IV fluids were warmed and where preoperative forced air warming had been utilised. However, shivering is multifactorial and not only related to thermoregulation (Chan, et al., 1989), but can occur with normothermia and in some instances is thought to be related to decreased sympathetic nervous system activity or anaesthetic drugs, amongst other possible

causes (Horn et al., 1998). The influence of warming interventions upon maternal comfort is unclear, however the ambient temperature of the operating theatre appears to be important in this context, partly due to the variations in ambient temperature seen in studies reporting varying effectiveness of warming upon thermal comfort. Further investigation into maternal warming and the impact upon neonatal outcomes, is required as benefits for neonates remain unclear from the synthesis of studies included in this systematic review (Munday, Hines, Wallace, et al., 2013). Therefore, neonatal outcomes, as well as maternal outcomes of shivering and thermal comfort, should be included as outcomes in future studies evaluating the effectiveness of maternal warming interventions.

Based upon the primary outcome of maternal temperature, and the reported decreased effectiveness of warming seen where women have received intrathecal opioids, notably morphine, (as addressed in Chapter 3), an observational study utilising a retrospective case-control design was conducted. The primary aim of this study was to investigate and establish whether there were differences in maternal temperature decline between women that receive, and those who do not receive, intrathecal morphine.

Chapter 5: Perioperative Hypothermia and Intrathecal Morphine

5.1 INTRODUCTION

The concept for this observational study arose from the literature (discussed in Chapter 2) which explored the phenomenon of hypothermia apparently associated with the administration of intrathecal morphine, the findings from the systematic review (Chapter 3) that intraoperative warming appeared to be less effective where intrathecal opioids were administered (Munday, Hines, Wallace, et al., 2013), and from my observations in the clinical area whereby there are cases of women receiving intrathecal morphine noted to experience a high degree of prolonged heat loss, together with symptoms of diaphoresis.

The study sought to compare temperature decline and hypothermia between women receiving intrathecal morphine (which can be considered standard care) and those who did not receive intrathecal morphine (commonly for reasons of allergy, patient preference due to unwanted side effects of morphine, or to avoid reactivation of the herpes simplex virus in known carriers). The study also sought to identify how many women, within the study population, experienced profound and prolonged hypothermia, with paradoxical symptoms (as described in Chapter 2). A further secondary aim was to consider any identifiable clinical factors associated with hypothermia in women undergoing caesarean section. Ethical approval for this study (as appropriate for a study deemed low-risk due to the data collection methods consisting of chart reviews) was obtained from the Mater Human Research Ethics Committee in May 2013 (see Appendix K), along with Research Governance approval (Appendix K). Following this, administrative ethical approval was obtained from Queensland University of Technology's Human Research Ethics Committee (see Appendix K).

Two methods of identifying eligible women were utilized. The register maintained by the Acute Pain Service (APS) was initially accessed to aid identification of women who had received spinal anaesthesia for caesarean section, with and without

intrathecal morphine. However, this register was found to be incomplete. Therefore, this necessitated the hand searching of the charts of all eligible women, identified as undergoing caesarean section under neuraxial anaesthesia via records maintained by the Health Records department. The necessity to review an extremely large number of charts to identify eligible participants resulted in data collection taking place over an extended period of time (12 months) from start to finish. Data collection was completed in May 2014.

MS Access ™ was used to develop a database, following the format of a hard copy data collection form (see Appendix L), in which to input data directly from patient charts. Data were collected by two researchers (myself, and a research assistant) and, after training, a sample of duplicate charts was reviewed to enable inter-rater reliability to be established (see accepted paper). A guide for data collection, for reference, for the use of the research assistant, was also produced (see Appendix M).

The study, as reproduced here, is the final version accepted by publication by the Journal of PeriAnesthesia Nursing, with some minor rewording for clarity.

5.1.1 Contribution of Authors

The author team for the manuscript presented here included J Munday, S Osborne and P Yates (see Statement of Contributions, Appendix N). I am identified as the principal and corresponding author, based on the criteria by the International Committee of Medical Editors (ICMJE 2016).

5.2 INTRATHECAL MORPHINE RELATED PERIOPERATIVE HYPOTHERMIA IN WOMEN UNDERGOING CAESAREAN SECTION: A RETROSPECTIVE, CASE-CONTROL STUDY

Abstract

Purpose

Rates of inadvertent perioperative hypothermia amongst women undergoing spinal anaesthesia for caesarean section are reported to be high. Intrathecal morphine has been noted to have a potentially potent effect upon thermoregulation. This retrospective case-control study sought to investigate the incidence of perioperative hypothermia in women undergoing caesarean section with and without intrathecal morphine and to describe any clinical factors associated with the condition, the identification of which would provide direction for nursing priorities in the care of the condition.

Methods

The charts of 358 women who had undergone emergency or elective caesarean section under spinal anaesthesia were reviewed: 179 having received intrathecal morphine and 179 having received spinal anaesthesia without intrathecal morphine (control group). SPSS version 22 was used for data analysis, including logistic regression to predict the outcome of hypothermia across the study population.

Findings

There was no significant difference ($p = 0.62$, 95%CI -0.09 – 0.15) in mean postoperative temperature for the morphine group (mean PACU arrival temperature 35.91°C, SD 0.59) and the no morphine group (mean PACU arrival temperature 35.88°C, SD 0.52). However, within groups, the temperature decline preoperatively to postoperatively was statistically (and clinically) significant.

Conclusion

The results refute the suggestion that intrathecal morphine contributes to greater core temperature decline in this population, however it does confirm that perioperative hypothermia is a prevalent concern for women undergoing caesarean section, and that pre-emptive measures should be routinely considered by healthcare providers.

Keywords: caesarean section, intrathecal morphine, observational, opioids, perioperative hypothermia.

Purpose

Perioperative hypothermia, in all surgical populations, is physiologically detrimental provoking a range of adverse side effects (Kurz, Sessler & Lenhardt., 1996; Beilin, et al., 1998; Scott & Buckland, 2006; Leslie, et al., 1995; NCCNSC, 2008; Reynolds, & Beckmann., 2008). Whilst there are reported high rates of hypothermia (defined as a core temperature < 36°C related to undergoing surgery under anaesthesia) (NCCNSC., 2008; Reynolds, et al., 2008) during and after spinal anaesthesia amongst women undergoing caesarean section, (Hess, Snowman & Wang., 2005) it is noted that intrathecal morphine may have a potentially potent effect upon thermoregulation, and that a small subset of women who receive intrathecal morphine develop particularly prolonged hypothermia. (Hess, et al., 2005; Wishaw, 1997; Hui, et al., 2006; Sayyid, Jabbour, & Baraka., 2003; Kavee., et al, 1991). This presents a challenge for healthcare providers caring for these women postoperatively.

Profound hypothermia after intrathecal morphine administration has been reported at temperatures as low as 33.1°C (Kosai, et al., 1992), however other reports have described a nadir of 33.2-34.9°C (Hess, et al., 2005; Ryan, et al., 2012; Bicalho, et al., 2006; Sayyid, et al., 2003; Kanawaza, & Okutani., 2015; Giladi, & Ioscovich., 2015). As opposed to the commonly experienced perioperative hypothermia, a prolonged episode of profound temperature drop is experienced (reportedly ranging from 2hrs (Hess, et al., 2005) to 19hrs (Kosai, et al, 1992) to return to normothermia). In these cases, diaphoresis (sweating) and a sensation of feeling hot is commonly described, and this is sometimes accompanied by nausea and itching, causing extreme discomfort. For women undergoing caesarean section, any

experience of perioperative hypothermia (whether this is prolonged and symptomatic as described above, or the commonly seen perioperative heat loss) can interfere with immediate postoperative recovery (Butwick, Lipman, & Carvalho, 2007).

The exact mechanism by which intrathecal morphine contributes to hypothermia is not definitively known (Butwick, et al., 2007). Core temperature, in all humans, is maintained within very narrow limits (Horn, et al., 2002) by the hypothalamus. The thermoneutral zone (also referred to as the inter-threshold range) (Buggy, & Crossley., 2000) – that is, the temperature range between which temperature receptors do not provoke the hypothalamus to initiate a 'too hot' or 'too cold' response - is tightly controlled within generally just a 0.4°C range (Buggy, & Crossley., 2000). Outside of this range both behavioural and autonomic responses are initiated to alter temperature. It is thought that cephalic (head wards) spread of the morphine contributes to prolonged hypothermia by (Hess, et al., 2005), altering the temperature set point, (Hess, et al., 2005; Kanazawa & Okutani, 2015) whereby the new upper temperature set-point (or threshold) triggering sweating (a 'too hot' response) is below the normal inter-threshold range (Bicalho, et al., 2006). Therefore sweating is seen at a hypothermic temperature.

The reduced benefit of active warming when spinal opioids have been administered has been suggested by a systematic review of warming interventions in this population (Munday., et al 2014) and other literature (Butwick, et al., 2006; Fallis, et al., 2006; Halloran, 2009). Evidence suggests that preoperative (Horn, et al., 2002) and intraoperative active warming, shown to improve maternal and neonatal outcomes, has been less effective where women have received intrathecal morphine (Hess et al., 2005; Butwick et al., 2007; Fallis, et al., 2006). In addition, conventional active warming strategies may have little benefit in profound and prolonged hypothermia, (Hess, et al., 2005; Ryan, et al., 2012; Sayyid, et al., 2003; Kosai, et al., 1992; Halloran, 2009) due to patients feeling hot and sweaty, despite being hypothermic, not tolerating warming. Case reports suggest pharmacological interventions utilizing benzodiazepines such as Lorazepam (Hess, et al., 2005; Ryan, et al., 2012) or opioid antagonists such as Naloxone (Wishaw, 1997; Sayyid, et al., 2003; Bicalho, et al., 2006; Kanazawaa & Okutani, 2015) can be helpful in the treatment of prolonged intrathecal morphine related hypothermia. Shivering and the return of cold sensation after the administration of Lorazepam has been described

(Hess, et al., 2005). The return of the perception of cold enables warming to be applied.

A small observational study of 100 patients reported incidence of hypothermia amongst women receiving intrathecal morphine for caesarean section was 32% and, within this figure, a subgroup was identified with an incidence of prolonged hypothermia (with a mean temperature of 34.9°C) of 6% and 7% (Hess, et al., 2005) Patients with prolonged hypothermia were symptomatic for between 120-360 minutes, however patients who were 'asymptomatic' but hypothermic returned to normothermia within 30 minutes postoperatively. A controlled trial also found that women receiving intrathecal morphine for caesarean section had significantly lower temperatures for up to 24 hours, as compared to those who received epidural morphine (Kavee, et al., 1991).

Prolonged hypothermia following intrathecal morphine administration for caesarean section has been observed anecdotally in the study hospital setting and is known to be uncomfortable for women and problematic for recovery room nurses and midwives to treat, however no figures exist to quantify this in the study hospital. This study aimed to, firstly, establish the incidence of perioperative hypothermia experienced by caesarean section patients receiving spinal anaesthesia with and without morphine to compare hypothermia incidence between these groups, and secondly, to examine the prevalence of prolonged, profound hypothermia. The study also intended to identify any surgical or intraoperative factors influencing hypothermia within this population.

Methods

A retrospective case-control design reviewed inpatient charts of eligible participants admitted between 2007 and 2014. Administration of intrathecal morphine (combined with intrathecal fentanyl and hyperbaric bupivacaine) is standard care in our institution; therefore the 'no morphine group' were selected first by identifying patients who, due to clinical reasons such as allergy, did not receive intrathecal morphine. This group was then matched with patients who did receive intrathecal morphine. Each element of the data collection tool was linked to relevant factors identified in the literature, such as age, body mass index (BMI), preoperative

temperature and surgery duration, as well as intraoperative interventions, and anaesthetic variables such as spinal block. An operational definition of profound hypothermia was established, also based on the literature (Hess, et al., 2005; Ryan, et al., 2012; Sayyid, et al., 2003; Kosai, et al., 1992; Halloran, 2009). Based on this operational definition, data were collected on shivering, nausea, vomiting, hypotension and sweating. The admission temperature on arrival to the Post Anaesthetic Care Unit (PACU) via aural canal Genius First Temp™ thermometers (with an accuracy of +/- 0.2°C between 36°C to 39°C and of +/-0.3 °C below 36°C) (Covidien, 2011) obtained by the registered nurses working in PACU, was considered to indicate perioperative thermal status and used to generate a categorical variable for perioperative hypothermia.

Women undergoing elective or emergency caesarean section under spinal anaesthesia (in a public tertiary hospital in South-East Queensland, Australia) were eligible for inclusion. Assuming a prevalence of hypothermia in both groups could be as high as 35%, based on earlier published rates of hypothermia receiving spinal anaesthesia for caesarean section (Hess, et al., 2005) and previous audits of hypothermia within adult (non-obstetric) patients at the study hospital, the required sample size to report a 95% confidence interval of 28-42% was 179 patients per group, allowing for ten cases of hypothermia per independent variable to enable the use of logistic regression. (Peduzzi, et al., 2006).

After training, inter-rater reliability was established between the two researchers using the kappa statistic to test agreement on key categorical variables (surgery status, intrathecal morphine status, intraoperative fluid warming, hypotension), and the intraclass correlation coefficient for continuous variables (age, PACU arrival temperature, PACU discharge temperature, parity), using SPSS™ (V15). Results were used to indicate if further training was required. Confidentiality was maintained: no identifiable patient data were retained. Ethical approval was obtained from the hospital and university human research ethics committees.

Descriptive statistics (using SPSS™ V15) assessed sample characteristics and summarised hypothermia incidence. Variables with a high amount of missing data were not considered further, however no cases were dropped completely due to missing data. Mean and standard deviations are reported for normally distributed continuous data, median and range for non-normally distributed continuous data, and

frequencies and percentages for categorical variables. The independent samples t-test was used to examine differences in means for normally distributed dependent variables. The paired samples t-test was used to evaluate postoperative temperature in relation to preoperative temperature. The Chi-squared test of independence (using Yates' Continuity Correction) was used to compare groups. One-way ANOVA was used to explore differences between groups in relation to independent variables with multiple categories. One-way analysis of covariance (ANCOVA) was used to examine mean PACU arrival temperature for both groups, with preoperative temperature as a covariate. A statistical significance level of $p = < 0.05$ was used. Correlation between continuous variables using Pearson product-moment correlation coefficient was checked prior to logistic regression, for which SPSS™ (V22) was utilised to investigate potential factors influencing the development of hypothermia.

Findings

A total of 358 charts of women undergoing spinal anaesthesia for elective or emergency caesarean section were included. Both groups were similar in relation to demographic and surgical variables (see Tables 1-3), apart from median surgical duration (in minutes) which was significantly longer in the no morphine group ($p = 0.04$) and intrathecal fentanyl dose (mcg), which was also significantly greater in the no morphine group ($p = 0.02$). Although statistically significant, it is unlikely that the small difference of only three minutes in median surgical duration between the groups has any clinical significance.

Table 1: Demographic variables

Variable	Morphine (n=179): Mean (SD) / number (%)	No Morphine (n=179): Mean (SD) / number (%)
Age (yrs)	30.6 (SD 5.6) (n=178)	30.5 (SD 6.2) (n-178)
Pre-pregnancy BMI	25.4 (SD 6.13) (n =174)	25.7 (SD 5.3) (n=168)
Pre-pregnancy weight (kg)	68.7 (SD 17.8) (n=145)	68.6 (SD 15.5) (n=144)
Height (cm)	162 (SD 7.2) (n=140)	163.3 (SD 7.3) (n=141)
Gestation (days)	264.1 (SD 20.1) (n=177)	265.1 (SD 17.7) (n=179)
Gravidity	3 (range 1-11) (n = 178)	3 (1-10) (n = 179)
Parity	2 (range: 1-8) (n = 177)	2 (1-8) (n = 178)

See Tables 2 & 3 (Supplementary Data – Appendix O)

Mean temperature and hypothermia incidence.

The small difference in mean postoperative (PACU arrival) temperature between groups (0.03°C) was not statistically significant (p = 0.62, 95%CI -0.09 – 0.15) with mean temperatures in both groups below the 36°C threshold (35.91°C SD 0.60 in the morphine group, versus 35.88°C SD 0.55 in the no morphine group). No significant association was found between morphine or no morphine and hypothermia status. (x2 (1, n= 358) = 0.18, p = 0.67, phi = -.028) Based on the odds ratio, the odds of women experiencing hypothermia in the morphine group was 0.90 times less than if they had not received intrathecal morphine, using the cut-off temperature of <36°C to indicate hypothermia. After adjusting for preoperative temperature, there was still no significant difference in mean PACU arrival temperature between groups: F (44, 247) = 0.005, p = 0.941, partial eta squared 0.00).

Table 4: Temperature: preoperative, PACU arrival and PACU discharge (°C)

Temperature (°C)	**Intrathecal morphine (mean, SD)**	**No intrathecal morphine (mean, SD)**
Preoperative	36.6 (SD 0.48) *n = 155*	36.5 (SD 0.43) *n=137*
PACU arrival	35.9 (SD 0.60)	35.9 (SD 0.55)
Ready to discharge from PACU	36.3 (SD 0.50) *n=169*	36.2 (SD 0.48) *n=162*
Temperature decline	0.65 (SD 0.65)	0.57 (SD 0.60)

Temperature decline.

Both groups displayed a statistically and clinically significant temperature decline between preoperative measurement to PACU arrival time (in the morphine group: t (154) = 12.4, p <0.001 two-tailed, and, for the no morphine group: t (136) = 11.2, p < 0.001 two-tailed), before an increase at 'ready to discharge' from PACU (see Table 4). The main effect comparing the two groups was not significant: F (1, 270) = 0.43, p = 0.52, partial eta squared = 0.002.

Overall, the entire study population (both groups together) experienced a statistically significant decrease in mean temperature (°C) (0.62°C, 95% CI 0.54-0.69). p<0.001, t (291) = 16.7) from the preoperative to postoperative phase (mean preoperative

temperature 36.5°C, SD 0.46, arrival to PACU 35.9°C, SD 0.58). However, the number of patients documented on the anaesthetic chart as having received any form of intraoperative warming was low (19%, n = 68), although, due to poor documentation, warming is likely to be under-reported. Active intraoperative warming could not be considered further due to the large amount of missing data (> 20%).

Prolonged intrathecal morphine related hypothermia

Only 8 patients experienced immediate postoperative hypothermia accompanied by sweating, nausea or vomiting, however two of these patients had received no intrathecal morphine. This small group represents 2% of the overall study population and therefore, little further investigation of this condition was conducted.

Anaesthetic and surgical factors associated with hypothermia.

Within the morphine group, differing morphine dosage of either 0-100mcg (n = 98, mean 36.0°C, SD 0.6), or 101-200mcg (n = 80, mean 35.9°C, SD 0.6) did not result in a significant difference in PACU arrival temperature (t (1.16, p = 0.25, two tailed). When categorised into dosage groups, fentanyl dosage did initially result in a statistically significant difference in mean PACU arrival temperature (see Table 5), with post-hoc comparisons (using the Tukey HSD test) indicating the mean temperature for 10mcg was significantly different than the other groups. However, the 10mcg group size was small (n = 15) and included one extremely low value (33.6°C). Although mean temperature for this group remains lower, when the analysis was re-run without this value, there was no significant difference between the groups: F (3, 341) = 1.5, p = 0.22, eta squared 0.01.

Table 5: Mean postoperative temperature and fentanyl dose

Fentanyl dose	Mean postoperative temperature (°C)
10mcg *	35.6 (SD 0.7)
15mcg	35.9 (SD 0.6)
20mcg	35.9 (SD 0.6)
25mcg	35.9 (SD 0.5)

*with outlier of 33.6°C removed

There was no significant association between the level of spinal anaesthetic insertion and postoperative hypothermia ($x2$ (2, n = 266) = 3.4, p = 0.18, phi = 0.11) or between the position of spinal anaesthetic administration (sitting or lateral) and postoperative hypothermia: $x2$ (5, n = 232) = 0.19, p = 0.67, phi = 0.53). Based on the odds ratio, the odds of developing hypothermia if receiving spinal anaesthesia in the sitting position was 1.29 times greater than if placed in the lateral position. Patients with pregnancy-induced hypertension (PIH) experienced higher mean PACU arrival temperatures with a mean temperature decline of 0.5°C, with a statistically significant higher mean preoperative temperature than those without the condition (see Table 6).

Table 6: Pregnancy Induced Hypertension and mean temperature

Variable	**Mean postoperative (PACU arrival) temperature** °C (mean, SD)	**Mean preoperative temperature** °C (mean, SD)
PIH	36.3 (SD 0.6)	36.8 (SD 0.4)
No PIH	35.9 (SD 0.5)	36.5 (SD 0.5)
P value	<0.001	0.005

Both groups had similar numbers of both emergency and elective patients (see Table 2). Differences in incidence of hypothermia between emergency and elective patients were investigated; a significant association was found between category of surgery and hypothermia status ($_X2$ (1, n=356) = 87 p = 0.03, phi = 0.16). Based on the odds ratio, the odds of women developing hypothermia was 0.52 times less likely if having an emergency rather than an elective caesarean section. Elective patients experience statistically significant greater temperature decline than emergency patients (see Table 7). Mean PACU arrival temperature differed significantly between elective and emergency patients, despite no significant difference in preoperative temperature between these groups. The magnitude of the difference in the means (0.21, 95% CI 0.09 to 0.32) was small (eta squared = 0.03). The statistically significant higher number of patients with PIH, (shown to have higher mean preoperative and postoperative temperatures) in the emergency population may contribute to the higher overall mean temperatures experienced by this group (see Table 7).

Table 7: Temperature outcomes: emergency and elective patients

Temperature outcome	Category		Mean difference [95% CI]	Sig
	Emergency	Elective		
Mean preoperative temperature (°C)	36.4 (SD 0.5)	36.5 (0.5)	0.04 [-0.06, 0.15]	0.4
Mean PACU arrival temperature (°C)	36.0 (SD 0.6)	35.8 (SD 0.5)	0.21 [0.09, 0.32]	0.001**
Postoperative hypothermia	80 (48%)	121 (64%)	n/a	0.03*
Temperature decline: preoperative temperature to PACU arrival (°C)	-0.53 (SD 0.6)	-0.69 (SD 0.6)	0.16 [0.01, 0.30]	0.03*
Pregnancy-induced hypertension (PIH)	26 (15.6%)	6 (3.2%)	n/a	0.001**

- significance < 0.05; ** significance < 0.01

Binary logistic regression indicates that BMI, category of surgery, PIH and preoperative temperature were significant predictors of postoperative hypothermia status.

Table 8: Predictors of postoperative hypothermia status

Variable	OR	95% CI	Significance (p value)
BMI	0.54	0.32- 0.91	0.02
PIH	0.2	0.06-0.6	0.004
Preoperative temperature	0.36	0.20-0.70	0.001

Discussion

A high incidence of postoperative hypothermia was found both in women who received intrathecal morphine, and those who did not, during spinal anaesthesia for caesarean section, with no significant difference in temperature decline or hypothermia incidence between groups. Within the group of patients who experienced hypothermia, this study suggests an incidence of prolonged hypothermia with paradoxical symptoms far less than Hess' work (Hess, et al., 2005), however this low incidence should be approached with caution (see Limitations). The observation of this clinically important phenomenon in practice suggests that it is more prevalent than the data indicates and that it may be better explored via a case series of already identified cases in this population and setting.

Although these results do not suggest a significant association between intrathecal morphine and maternal postoperative temperature, nor that opioid dosage amounts or spinal insertion level or position appear to influence postoperative temperature, they do establish a statistically and clinically significant temperature decline across the whole study population of women receiving spinal anaesthesia for caesarean section. While the 0.6°C temperature decline may appear small, it is clinically significant because it is sufficient to drop mean temperature from what is defined as a normothermic temperature to mild hypothermia (below 36°C) (NCCNSC, 2008; Reynolds, et al., 2008).

Results of this study, and other work (Bamgbade, 2012), suggests that preoperative temperature measurement is poorly implemented in many settings including obstetric theatres. This is despite its importance in identifying thermal status, which enables perioperative staff to implement pre-emptive action, as appropriate, to prevent further temperature decline (or, indeed, increase), with the aim of maintaining temperature within normal ranges. This reflects the position of the widely cited National Institute for Health and Care Excellence (NICE) guidelines for inadvertent perioperative hypothermia which recommend preoperative thermal status monitoring prior to patient transfer to the operating suite, but stops short of making any recommendations for obstetric patients (NCCNSC, 2008). The ASPAN Evidence-Based Clinical Practice Guideline for the Promotion of Perioperative Hypothermia also emphasise the importance of measuring patient temperature on admission and assessing the patient's thermal comfort level (Hooper, et al., 2010). Given the high rates of perioperative hypothermia reported in this population, it appears reasonable that this recommendation be extended to the obstetric population undergoing caesarean section.

Similarly, intraoperative temperature monitoring for obstetric patients is not routine in our institution, despite patients routinely receiving intravenous fluid warming. This echoes findings from a European survey of intraoperative temperature monitoring and management, which indicated that in many instances active warming was instigated without temperature monitoring (Torossian, 2008). Again, the requirement for intraoperative temperature monitoring, as recommended by NICE, for all patients with an anaesthesia time exceeding 30 minutes, seems reasonable to apply to the population of women undergoing caesarean section (NCCNSC, 2008).

The extent of temperature decline experienced by elective patients also suggests that focus needs to be directed towards planning effective thermal care for this group. While the urgency often associated with emergency caesarean section can impede preoperative thermal care planning, processes should be established for routine elective surgery that do facilitate thermal care planning. Other work has suggested that active warming for this population is under-utilised (Woolnough, et al., 2009; Sultan, et al., 2015), despite recommendations to the contrary (Sultan, et al., 2015; Munday, et al., 2014). Although incomplete documentation impedes the investigation of the proportion of patients that did receive intraoperative warming in this study, the temperature decline evident in both groups suggests that more can be done to improve perioperative heat loss. Perioperative nurses and the entire perioperative team have a part to play in this process.

Limitations

Although this study design, by its nature, lacks control of potentially confounding factors not documented in patient charts (for example ambient temperature), data included a wide range of demographic and intraoperative variables. Although intraoperative temperature data would be valuable, PACU arrival temperature, which appears to be measured consistently on arrival to PACU, was considered an indicator of immediate postoperative temperature, to identify hypothermia and intraoperative temperature decline. Measurement time points for preoperative temperatures also varied. In order to reduce bias during data collection, inter-rater reliability was established between the two researchers responsible for data collection. This type of study cannot account for some contributing external and environmental factors, such as a cool ambient operating theatre temperature (21.3°C +/- 0.3°C), which has been identified as a significant predictor of inadvertent hypothermia, as opposed to warmer ambient temperatures (Frank, et al., 1992). Ambient temperature should certainly be an independent variable in controlled study designs considering body temperature.

Conclusions

The evidence appears to refute the suggestion that intrathecal morphine contributes to greater core temperature decline in this population, and confirms that perioperative hypothermia is a prevalent concern for women undergoing caesarean section. It also reiterates the importance of nurses caring for perioperative patients taking pre-emptive measures including the routine measurement of preoperative temperature and appropriate resultant action. Further work is needed to explore the phenomenon of prolonged intrathecal morphine related hypothermia with paradoxical symptoms, in relation to identifying associated factors that may contribute to this condition and therefore aid in perioperative care planning.

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5.3 CHAPTER SUMMARY

The evidence from this study suggests that the incidence of perioperative hypothermia is of equal concern for women undergoing spinal anaesthesia for caesarean section, irrespective of whether they receive intrathecal morphine. Both groups experienced a statistically significant temperature decline of 0.62°C. While this difference is less than a degree, it is also clinically significant, and in many patients this will result in the change in status from being normothermic to hypothermic. In patients who are already hypothermic when surgery commences, this temperature decline is even more significant.

While the systematic review results indicated that intraoperative warming was less effective in the studies where intrathecal opioids had been administered (Munday, Hines, Wallace, et al., 2013), no studies were identified that tested preoperative warming where participants had received intrathecal opioids (in particular, morphine), although preoperative warming had been found to be of benefit to those populations tested, who did not receive intrathecal opioids (Munday, et al., 2014). Despite the findings from the systematic review suggesting that preoperative warming is of benefit, and the findings from this observational study indicating that perioperative hypothermia is a problem in the majority of women undergoing caesarean section, there remains a gap in the science regarding the duration and timing of active warming strategies for optimal thermal care of women undergoing caesarean section, particularly those receiving intrathecal morphine. In Chapter 6, I will present the methods and findings from a randomised controlled trial, which tested a preoperative warming regime, in the population of women receiving intrathecal morphine for caesarean section, for the primary outcome of maternal temperature decline.

Chapter 6: Preoperative Warming for Maintenance of Normothermia in Women Receiving Intrathecal Morphine for Caesarean Section.

6.1 INTRODUCTION

Results from the systematic review and the observational study presented in the earlier chapters informed the development of a randomised controlled trial, which tested the effect of preoperative warming upon maternal temperature in women receiving intrathecal morphine for caesarean section. The impetus for this study arose from the following observations: firstly, the systematic review suggested that warming may be less effective where intrathecal opioids, specifically morphine, had been administered, however these results pertained to intraoperative warming only. Preoperative warming in the context of intrathecal opioids for caesarean section had not been tested, although preoperative warming appeared to be effective at reducing maternal temperature decline where opioids had not been given. Secondly, results from the observational study suggested that there was significant temperature decline in women whether they received intrathecal morphine or not, indicating that effective interventions to reduce this decline are needed. Thirdly, this randomised controlled trial aimed to establish both the effectiveness of a period of preoperative warming that was feasible and practical for integration into the perioperative pathway. The duration and timing of preoperative warming was based upon relevant literature. The approach took into consideration the demands of perioperative routines as anecdotal evidence from the practice area suggested that longer durations of preoperative warming would be hard to achieve in the current perioperative system of care. Guidance for general adult preoperative warming suggests that an hour of preoperative warming be applied (NCCNSC 2008), however recent studies of preoperative warming, in other populations have found shorter periods to be effective (Horn et al., 2012). Intrathecal morphine administration is part of standard care for

women undergoing caesarean section, not only in the institution where the study was conducted but also in many healthcare facilities due to the benefits gained from prolonged postoperative analgesia. Therefore adequate methods of protecting normothermia for these women are required.

The paper presented here is a version accepted for publication. Also included Appendix P are the Mater Human Research Ethics Approval, Mater research governance approval, Queensland University of Technology administrative ethics approval. Also included as appendices are the participant information and consent form (Appendix Q), the anaesthetic protocol (Appendix R) and data collection forms (Appendix S). As well as the intention-to-treat analysis reported in the paper for publication, per protocol analysis was also undertaken. This is reported in Appendix T.

6.1.1 Contribution of Authors

I was the primary investigator, responsible for designing the research protocol, data collection, data analysis and writing up the final manuscript. Dr Sonya Osborne was involved in reviewing the research protocol, review and discussion of data analysis procedures and reviewing the final manuscript. Professor Patsy Yates also reviewed the research protocol and the final manuscript (see Statement of Contributions, Appendix U). To reduce variability in practice, and therefore potential confounding, a protocol of the anaesthetic and perioperative management of patients enrolled in the study was deemed necessary. This was developed in consultation with anaesthetic medical staff, namely Dr David Sturgess, but also with the support of the Deputy Director of Anaesthesia, Dr Simon Maffey, and widespread consent from other anaesthetic medical staff. Support from the study was also obtained other relevant nursing, midwifery, theatre and medical staff. Education sessions were conducted for ward and theatre staff, prior to the commencement of the study, and resource folders were made available for reference. Statistical advice was obtained from Lee Jones and Edward Gosden (Research Methods Group, Queensland University of Technology).

6.2 SUBMITTED PAPER: PREOPERATIVE WARMING VERSUS NO PREOPERATIVE WARMING FOR MAINTENANCE OF NORMOTHERMIA IN WOMEN RECEIVING INTRATHECAL MORPHINE FOR CAESAREAN DELIVERY: A SINGLE BLINDED, RANDOMISED CONTROLLED TRIAL

Abstract

Introduction

Rates of hypothermia for women undergoing spinal anaesthesia for caesarean delivery are high and prevention is desirable. This trial compared the effectiveness of pre-operative warming versus usual care amongst women receiving intrathecal morphine, which is thought to exacerbate perioperative heat loss.

Methods

A prospective, single-blinded, randomised controlled trial compared 20 minutes of forced air warming (plus intravenous fluid warming) versus no active preoperative warming (plus intravenous fluid warming) in 50 healthy American Society of Anesthesiologists (ASA) graded II women receiving intrathecal morphine for elective caesarean delivery. The primary outcome of maternal temperature change was assessed via aural canal and bladder temperature measurements at regular intervals. Secondary outcomes included maternal thermal comfort, shivering, mean arterial pressure, agreement between aural temperature, and neonatal outcomes (axillary temperature at birth, Apgar scores, breastfeeding and skin-to-skin contact). The intention-to-treat population was analysed with descriptive statistics, general linear model analysis, linear mixed model analysis, Chi-square test of independence, Mann-Whitney, and Bland Altman analysis. Full ethical approval was obtained, and the study was registered on the Australia and New Zealand Clinical Trials Registry (Trial No: 367160, registered at http://www.ANZCTR.org.au/).

Results

Intention-to-treat analysis (n=50) revealed no significant difference in aural temperature change from baseline to the end of the procedure between groups: F (1,

47) = 1.2, p =0.28. There were no other statistically significant differences between groups in any of the secondary outcomes.

Conclusions

A short period of pre-operative warming is not effective in preventing intraoperative temperature decline for women receiving intrathecal morphine. A combination of preoperative and intraoperative warming modalities may be required for this population.

Introduction

Women undergoing caesarean section are a vulnerable but often overlooked population in guidelines for perioperative temperature management. Inadvertent perioperative hypothermia, defined as the unintentional cooling of core temperature to below 36ºC during surgery (NCCNSC 2008) has detrimental physiological effects which have been well-studied in the non-pregnant population. These include increased blood loss (Rajagopalan, et al., 2008), higher wound infection rates (Kurz, et al., 1996), immune function suppression (Beilin, et al., 1998), prolonged drug action (Heier & Caldwell, 2006; Leslie, et al., 1995), increased duration of recovery stays (Lenhardt, et al., 1997) and increased hospital stay (Kurz, et al., 1996), increased costs (Mahoney & Odom, 1999), shivering (Liu & Luxton, 1991; Roy, et al., 2004) and, importantly, discomfort. Impacts upon neonatal outcomes, such as temperature at birth (Horn, et al., 2002), umbilical vein (Horn, et al., 2002), and arterial pH and Apgar scores (Yokoyama, et al., 2009) have been demonstrated in some studies as well a relationship between neonatal hypothermia and hypoglycaemia (Baker & Lawson, 2012). Hypothermia is often undetected until the postoperative phase, causing significant disruption to postoperative care, as well as maternal-newborn bonding and feeding, whilst rewarming is applied.

Rates of perioperative hypothermia amongst women undergoing caesarean under spinal anaesthesia have been estimated as being as high as between 32% (Hess, et al., 2005) to 80% (Chakladar, et al., 2011). In addition, perioperative hypothermia appears to be intensified by intrathecal morphine (Cobb, et al., 2016 ; Halloran, 2009; Hess, et al., 2005; Hui, et al., 2006). Since, in clinical practice, spinal

anaesthesia, commonly utilising intrathecal morphine, often comprises standard care for this population, it is important that health care providers establish pre-emptive measures to reduce the occurrence of hypothermia, shifting the emphasis from treatment to prevention for all women undergoing caesarean delivery.

Guidelines for the general adult population advise 30 minutes of preoperative warming (NCCNSC 2008). A shorter period may be more clinically acceptable and practical, while still reducing intraoperative core temperature decline. Horn et al. tested passive warming versus 10, 20 or 30 minutes of preoperative forced air warming, in a randomised controlled trial of 200 patients undergoing laparoscopic surgery under general anaesthesia, finding that 10 minutes of preoperative warming resulted in significantly improved core temperature (Horn, et al., 2012). An optimum warming period of 20 minutes was recommended where clinically possible (Horn, et al., 2012). Fifteen minutes of preoperative warming before induction of epidural anaesthesia, plus continuation of forced air warming during surgery, has also shown efficacy at reducing hypothermia in a population of women receiving epidural anaesthesia but who did not receive opioids (Horn, et al., 2002).

This single blinded, randomised controlled trial compared the effect of a period of 20 minutes of preoperative forced air warming alongside intraoperative intravenous (IV) fluid warming with usual clinical care (IV fluid warming and no preoperative forced air warming) in a population of women receiving intrathecal morphine during elective caesarean delivery on the primary outcome of maternal temperature change from baseline to the end of the procedure. Secondary outcomes – for exploratory analysis only - included temperature decline assessed over time, hypothermia, maternal thermal comfort, mean arterial pressure (MAP), shivering, agreement with aural canal and bladder temperature measurements, neonatal axillary temperature at birth, Apgar scores at 1 and 5 minutes, skin-to-skin contact at birth, breastfeeding at birth and upon discharge from hospital and incidence of wound complications.

Methods

Study Design

Women with singleton pregnancies booked for elective caesarean delivery at term under spinal anaesthesia with intrathecal morphine were enrolled in this pragmatic,

single-blinded randomised controlled study, following hospital and university ethics approval, and informed consent. Exclusion criteria included known allergy to morphine, known impaired thermoregulation or thyroid disorders, vascular disease or poor cutaneous perfusion, ASA score >II, history of preeclampsia or eclampsia, planned Intensive Care Unit (ICU) admission, tympanic membrane/aural canal that was not visible on otoscopy and baseline temperature >37°C. The study was registered on the Australia and New Zealand Clinical Trials Registry (Trial No: 367160, registered at http://www.ANZCTR.org.au/ on 10th October 2014 by the principal investigator Judy Munday).

Study Protocol

After informed consent, and otoscopy, participants were randomly assigned to either the control or the intervention group. The randomisation schedule was computer–generated, utilising fixed-size blocks (at www.randomisation.com) of five per block and placed within sequentially numbered opaque envelopes. An independent coordinator generated the allocation sequence, and allocation to groups was concealed from the blinded outcome assessor.

Participants in the control group received usual care consisting of no active warming during the admission and preoperative period. Participants in the intervention group received 20 minutes of full body preoperative warming in which perioperative midwives independent of the study applied a forced-air warming device (Cocoon™) set to 43°C in the preoperative waiting area, prior to entering the operating room for induction of spinal anaesthesia. The investigator remained in the operating theatre and did not access the preoperative waiting area to ensure blinding. A delay of more than 20 minutes between the end of the preoperative warming and transfer to theatre was considered a protocol deviation. Patients were monitored during the intervention to assess for adverse side effects related to warming, such as diaphoresis or nausea and vomiting.

All women received intravenous fluid warming (compound sodium lactate) warmed to 38.5°C (via Biegler™ fluid warmer), were covered with a warmed cotton blanket and surgical drapes, and received standardized intraoperative anaesthetic medication and intravenous fluids. After induction of spinal anaesthesia, a temperature sensing

indwelling urinary catheter (Mon-a-Therm™) was inserted. All patients received spinal anaesthesia (or combined spinal-epidural anaesthesia with no opioids via the epidural catheter) in the sitting position at the L3-4 interspace, with 2.2 to 2.4mls hyperbaric 0.5% bupivacaine, intrathecal morphine 100mcg, and intrathecal fentanyl 15 to 20mcg. Block height was tested using ice, and the procedure commenced once a sensory block above T4 was achieved. Intravenous carbetocin 100mcg was administered at delivery. Rectal paracetamol 1g and diclofenac 100mg were administered at the end of the procedure. Variations to the protocol were documented and recorded. Ambient preoperative holding bay and operating room temperature was recorded via thermostat. At the end of the procedure, all patients were covered with a warmed cotton blanket and a reflective foil blanket, prior to transfer to PACU. If temperature decline, or temperature $\leq$ 35.5° C (as per institutional guidelines), shivering or cold discomfort was experienced in PACU, further warmed blankets were offered and/or forced air warming commenced as per routine care.

Maternal temperature was measured using both a calibrated Genius™ aural canal thermometer (cited as reading a mean of -0.4° C less than pulmonary artery measurement) (Robinson, Charlton, Seal, Spady, & Joffres, 1998) and Mon-a-Therm™ indwelling urinary catheterization (cited as providing accuracy to within 0.1° C of pulmonary artery measurement) (Russell & Freeman, 1996) at the following time points: baseline, pre-spinal, post-spinal, every 15 minutes and at the end of the procedure, on arrival to PACU, then every 15 minutes until ready for discharge from PACU. Maternal thermal comfort was measured using a 100mm Visual Analogue Scale (VAS), used in a number of studies measuring patient thermal comfort (Buggy & Crossley, 2000; Fallis, et al., 2006; Fossum, Hays, & Henson, 2001; Sessler & Ponte, 1990; Wilson & Kolcaba, 2004). Shivering was assessed via a three-point scale used in previous studies in this population (Saito, Sessler, Fujita, Ooi, & Jeffrey, 1998; Woolnough, Allam, et al., 2009) in the absence of a validated shivering scale. Mean arterial pressure (MAP) was measured at baseline, pre-spinal, post-spinal and at the end of the procedure, however only baseline, pre-spinal and post-spinal measurements were analysed due to the individual difference in the use of vasopressors in response to clinical need; which was not specified in the anaesthetic protocol. An independent midwife assessed neonatal axillary temperature, and Apgar scores, at 1 and 5 minutes after birth. Duration of skin-to-

skin at birth, feeding intention, breastfeeding and timing of feed at birth were recorded, as well as breastfeeding at 10 days post-natally which was determined retrospectively from the Universal Postnatal Contact Survey. Wound infection and dehiscence upon hospital discharge, and patient concerns with the post-natal wound (at 10 days) were also determined via chart review. Demographic data collection included maternal age, parity and gravidity. Surgical variables such as intraoperative blood loss, volume of intravenous fluid infusion, anaesthetic medication (including any which deviate from the agreed protocol) duration of procedure, preoperative and operating room (OR) ambient temperature were also recorded. This manuscript adheres to the CONSORT criteria for the reporting of RCTs (Ioannidis et al., 2004).

Statistical Analysis

Descriptive statistics were generated to summarize sample characteristics, and hypothermia prevalence. Data are expressed as means and standard deviations, median and range or as frequencies and percentages as indicated. A general linear model was used to assess the primary outcome of aural temperature change between groups, with adjustment for baseline temperature and surgery duration.

An exploratory analysis of secondary outcomes was undertaken, using linear mixed model analysis (to allow for fixed effects of baseline temperature, time and group, and a random intercept for repeated measures) for aural temperature decline from immediately after spinal insertion until the end of the procedure. Linear mixed model analysis was also used to assess thermal comfort between groups at repeated time points. Pearson Chi-Square test of independence with Continuity Correction was used to analyse hypothermia incidence, shivering and neonatal outcomes, with the Mann-Whitney U Test used for non-parametric mean arterial pressure data. Bland-Altman analysis (using MedCalc™) examined agreement31 between aural canal and bladder temperature, and to provide a means to establish the accuracy of the aural canal measurements used for the primary analysis. SPSS™ software (version 22) was utilised for all other data analysis: $p < 0.05$ was considered statistically significant for the primary outcome, and $p < 0.01$ for the secondary outcomes.

All analyses were performed on the Intention-to-Treat (ITT) population, which included all participants in the groups to which they were assigned, irrespective of protocol deviations.

A required sample size of 15 participants in each group was calculated, based on a repeated measures design with the initial temperatures being the same and the temperature decline being 0.4°C greater in the unwarmed group than the warmed group 45 minutes after commencement of surgery. A standard deviation of 0.4°C was used in the calculation, based on the data reported by Chung et al. (Chung, et al., 2012). A type I error rate of 0.05 and a power of 90% were specified. The sample size was inflated from a total of 30 to a total of 50 to allow for attrition.

Results

Patients were enrolled in the study between February 2015 and February 2016. All 50 patients completed the study (Figure 1), however there were 13 protocol deviations: seven in the preoperative warming group and six in the control group. Three patients in the pre-operative warming group had suspected bladder injury and received methylene blue dye; from the point of this occurrence bladder temperature for these patients was disregarded.

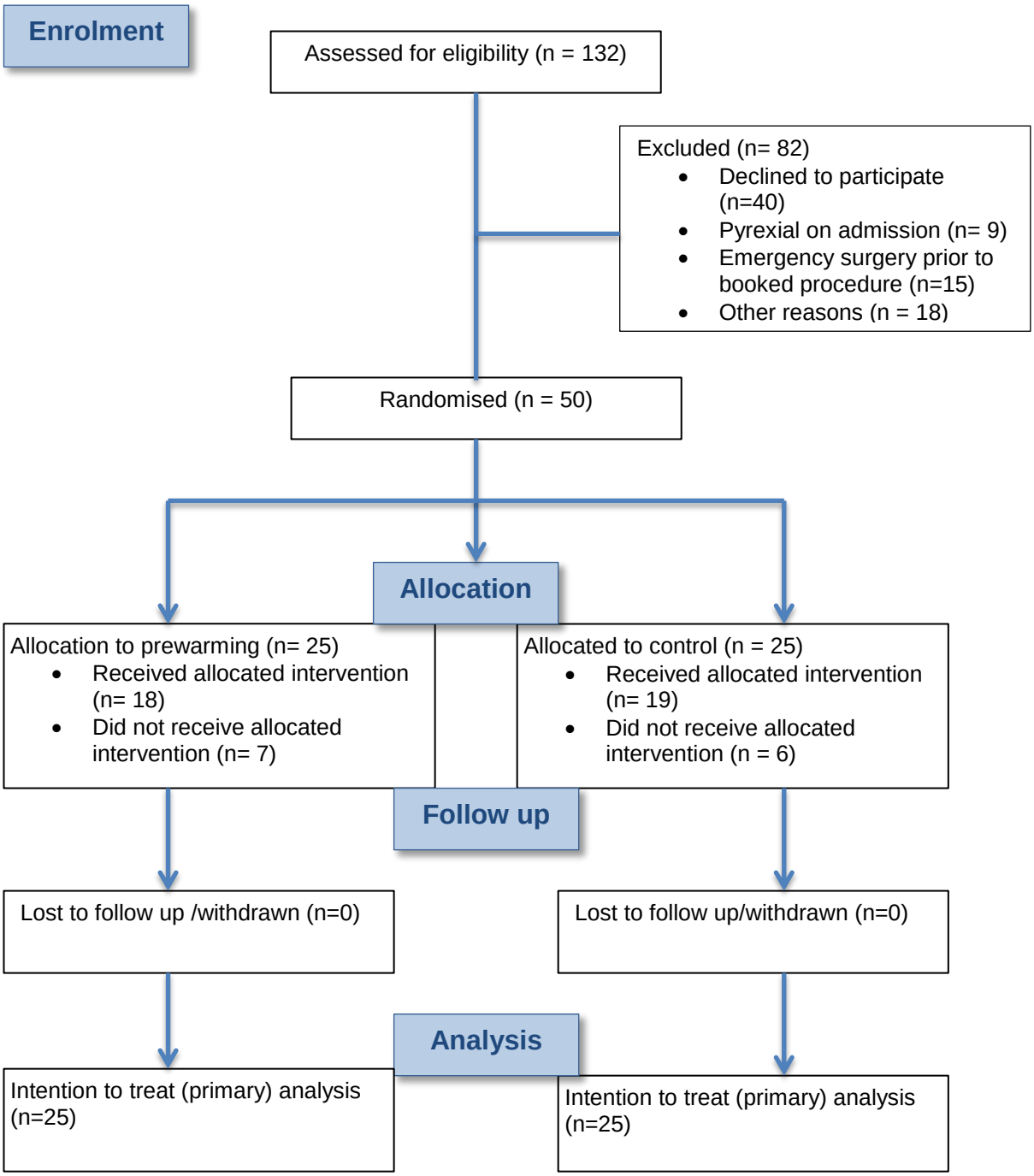

Figure 1: Study Flow-chart

Maternal baseline characteristics, as well as surgical and anaesthetic variables, were similar across treatment groups apart from baseline temperature (Table 1). In the warming group, four patients experienced sweating. Due to this, one patient ceased the warming period two minutes early by request. Nil other adverse events related to the warming intervention were reported.

Table 1: Maternal baseline, surgical and anaesthetic data

Variable	**Pre-operative warming: median, (range) (n=25)**	**Control: mean, SD/median, range (n=25)**
Age (yrs)	31 (23-41)	36 (19-40)
BMI	22.9 (16.2-38.2)	23.8 (17.6-40.3)
Gravidity	2 (1-7)	2 (1-6)
Parity	2 (1-5)	2 (1-5)
ASA I **ASA II**	21 4	19 6
Estimated blood loss (mls)	400 (200-700)	400 (200-600)
Surgical duration (mins)	46 (31-76)	46 (27-72)
Intraoperative Intravenous Fluid (mls)	1500 (800-2100)	1500 (800-2050)
Baseline temperature (°C)	36.6 (35.7-36.9)	36.8 (35.9-36.9)
Mean arterial pressure (MAP)	86 (69-100)	85 (71-96)
Spinal Time (mins)	12 (6-31)	14 (8-22)
Clean up time (mins)	9 (4-15)	10 (5-14)
Preoperative ambient temperature (°C)	23 (22-25)	24 (23-26)
OT Ambient Temperature (°C)	21.4 (20.2-23)	21.5 (20.6-22.6)

BMI: Body Mass Index; ASA: American Society of Anesthesiologists; MAP: mean arterial pressure; OR: operating room

Primary Outcome

Intention-to-treat analysis revealed no significant difference in aural temperature change from baseline to the end of the procedure between groups: F (1, 47) = 1.2, p =0.28, partial eta squared = 0.03) (Table 2).

Table 2: Temperature change (°C): baseline-end of procedure and hypothermic patients at each time point

	Temperature change °C (baseline – end of procedure): mean (SD) number		
	Preoperative warming	**Control**	**P value**
Intention-to- treat	0.5 (SD 0.32) (n=25)	0.7 (SD 0.57) (n=25)	0.28
Hypothermic patients (by group) at each time point			
	Intervention (n=25)	**Control (n=25)**	
Baseline	3 (12%)	1 (4%)	
Pre Spinal	0	0	
Post Spinal	0	0	
OR 15 minutes	4 (16.7%)	6 (25%)	
OR 30 minutes	6 (24%)	9 (36%)	
OR End Procedure	11 (44%)	12 (48%)	
PACU Arrival	12 (48%)	16 (64%)	

Hypothermia: defined as a temperature of <36°C

Secondary outcomes

Although the preoperative warming group experienced higher intraoperative mean temperatures, from the insertion of spinal anaesthesia until 30 minutes, this was not statistically significant and by 45 minutes temperatures in both groups were the same, when analysed using linear mixed model analysis, and controlling for baseline temperature (Figure 2). There were no statistically significant differences in hypothermia incidence between the groups (see Table 2).

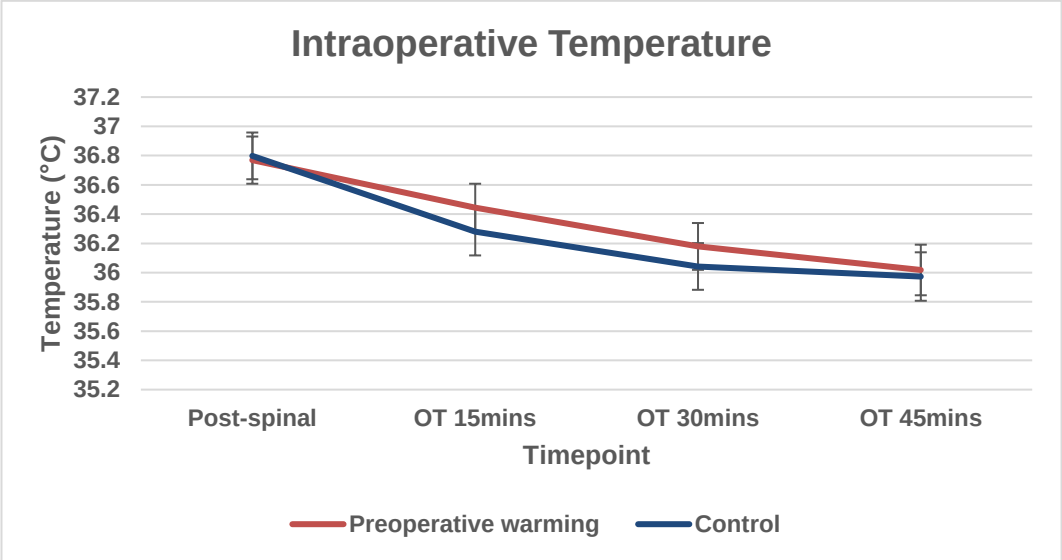

Figure 2: Intraoperative temperature (°C)

Maternal thermal comfort did not differ between groups at any time point (see Table 3). There were no clinically significant differences in MAP between groups or differences in postoperative outcomes (see Table 3). No patients experienced wound infection or dehiscence, assessed at discharge, in either group. On follow-up, one patient in the control group had a post-natal wound infection (10 days post-natally). Neonatal outcomes were also similar between groups (Table 3).

Table 3: Secondary Maternal and Neonatal Outcomes

Variable	Preoperative warming (n=25)	Control (n=25)	P value
Mild shivering*	3 (12%)	8 (32%)	0.09
Intense Shivering	0	3 (12%)	n/a
Any shivering*	3 (12%)	8 (32%)	0.09
MAP (Pre-spinal)#	97 (70-113)	97 (84-116)	0.69
MAP (Post-spinal)#	89 (68-112)	85 (56-118)	0.03
Overall maternal thermal comfort	5.4 (95%CI 5.1-5.7)	5.2 (95%CI 4.9-5.5)	0.58
PACU: arrival to ready to discharge (mins)	37 (30-76)	39 (27-81)	n/a
Warmed in PACU	17 (68%)	20 (80%)	0.52
Neonatal outcomes			
Axillary temperature (°C)**	36.8 (36.0-37.3)	36.6 (36.2-37.3)	0.26
Apgar at 1 min# ***Apgar 7*** ***Apgar 8*** ***Apgar 9*** ***Apgar 10***	 1 (4%) 4 (16%) 20 (80%) 0	 1 (4%) 3 (12%) 20 (80%) 1 (4%)	0.92
Apgar at 5 mins## ***Apgar 8*** ***Apgar 9*** ***Apgar 10***	 1 (4%) 24 (96%) 0	 0 24 (96%) 1 (4%)	0.74
SCN admission **ICN admission**	0 0	0 1	n/a 1
Respiratory distress	3 (12%)	5 (20%)	0.7
Intention to breastfeed	21 (84%)	23 (92%)	0.3
Breastfed at delivery	21 (84%)	22 (88%)	0.5
Skin-to-skin >30 minutes	12 (48%)	7 (28%)	0.23
Breastfed 10 days postnatally	13 (81%)	17 (85%)	1

* median (range) # number (%) **Fisher's Exact Test, ## median, range, *** Estimated marginal means, linear mixed model analysis, SCN: Special Care Nursery, ICN: Intensive Care Nursery

Bland-Altman analysis indicated that, apart from one outlier, differences between aural canal (Genius™) and bladder (Mon-a-Therm™) temperature measurement devices appear to be consistent as temperature changes. The mean difference between devices was 0.04°C (SD 0.25). The limits of agreement ranged from 0.93—0.86°C, however only two paired measurements exceeded a difference of 0.5 °C, conventionally cited as a clinically acceptable measurement variation (see Figure 3).

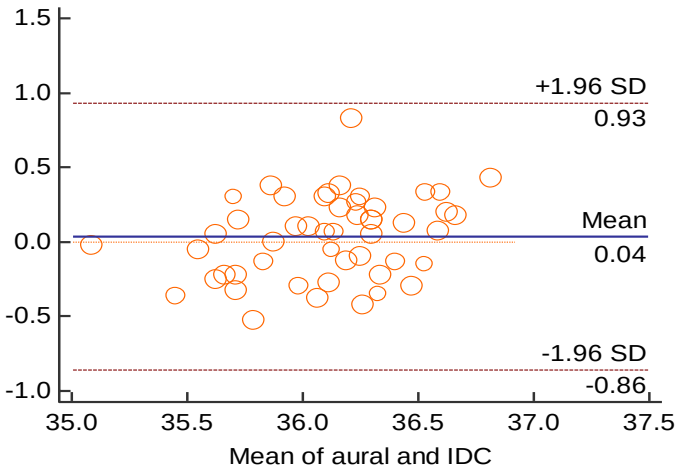

Figure 3: Bland-Altman Plot – Agreement between aural (Genius™) and bladder (Mon-A-Therm™) temperature

Discussion

Twenty minutes of full body preoperative warming, prior to spinal anaesthesia with intrathecal morphine for caesarean delivery, does not result in a significant decrease in intraoperative maternal temperature decline. Despite the increased core to periphery heat gradient that is proposed to result from preoperative warming (Horn, et al., 2002), by the end of the procedure both groups experienced temperature decline with similar end of procedure temperatures.

The results of our study contrast with Horn et al.'s findings that 15 minutes of upper body preoperative warming 43°C, continued intraoperatively, resulted in over 1°C difference between control and intervention group at the end of surgery, in favour of warming (Horn, et al., 2002). However, ambient temperature was higher in Horn's study, and surgical duration was slightly less than our study (Table 1). In addition,

their population received epidural anaesthesia with no opioids, which may contribute to the marked differences between their warmed and unwarmed groups (Horn, et al., 2002). Similarly, De Bernardis et al. also found temperature declined less when women received pre-operative warming that continued intraoperatively, (versus the control group receiving IV fluids warmed only to 37°C). All patients received spinal anaesthesia with 80mcg intrathecal morphine (de Bernardis, Siaulys, Vieira, & Mathias, 2015).

When considered in conjunction with the results from other comparable studies (Chung, et al., 2012; de Bernardis, et al., 2015; Horn, et al., 2002) several key variations appear important: the use (and dose) of intrathecal morphine, surgical factors including ambient temperature and surgical duration, and the use of pre-operative strategies that are both multi-modal and continued intraoperatively. Although it has been proposed that increased heat loss may occur with intrathecal morphine due to cephalic spread decreasing the temperature set-point, the reasons for this remain unconfirmed. Given current evidence, it cannot be said with certainty that intrathecal morphine blunts the response to warming.

Both groups in our study received IV fluid warming as per National Institute for Health and Care Excellence (NICE) guidelines that fluids of $\geq$500mls should be warmed to 37°C or more) (NCCNSC 2008), in the form of crystalloid co-loading at the time of spinal anaesthesia, as is usual care in our institution. This may help to maintain temperature during the period of intravascular volume shift that occurs during spinal anaesthesia (Cobb, et al., 2016). However, it is evident that IV fluid warming alone is not sufficient to prevent hypothermia in most patients, as indicated by the incidence of hypothermia in the control group in this study, again further suggesting that multi-modal interventions are likely to be of the most benefit (Cobb, et al., 2016)

Both researchers and clinicians have questioned whether forced air warming is tolerable or practical for obstetric patients (Chakladar & Harper, 2010; Petsas, et al., 2009). While this study did not assess tolerability in any meaningful way beyond recording adverse events related to warming, or patient symptoms of sweating, nausea or discomfort, it appears that patients in this study largely found the duration and 43°C setting tolerable. Only one patient asked to cease the intervention two minutes early, which compares favourably with results from Fallis et al.'s study of

upper-body intraoperative forced air warming, where 14 patients decreased the temperature of the forced air warmer from 43°C to a lower setting (Fallis, et al., 2006). Research into obstetric patient's preferences for warming interventions may be warranted.

The intensity and incidence of shivering may indicate the severity of hypothermia. In our study, no pre-operatively warmed patients, as opposed to 3 patients in the control group, experienced severe shivering. Warmed IV fluids were found to be effective at reducing shivering in recent meta-analysis (Munday, Hines, Wallace, et al., 2013). Non-thermogenic factors, such as catecholamines resulting from pain or anxiety, may also contribute to shivering (Alfonsi, 2003; Chan, et al., 1989), and larger studies of the impact of combined warming strategies incorporating pre-operative warming upon shivering are warranted.

This study was designed to test a pragmatic approach to warming by using a short preoperative full body warming regime, based on evidence of the optimal duration of effective preoperative warming (Horn, et al., 2012; Horn, et al., 2002). Warming was applied in the preoperative waiting area before women entered the OR. Our study protocol specified no greater than a 20 minute time delay between the end of the warming regime and entry to the OR but some participants experienced longer delays, which reduced power of the study to detect a difference between groups. The benefits of preoperative warming may be evident if warming is continued into the OR, through induction of neuraxial anaesthesia, through the commencement of the surgical skin preparation (Chung, et al., 2012; Horn, et al., 2002).

The use of aural canal thermometry is not without controversy, and that disagreement exists as to the accuracy of this method. However, this method is not invasive and therefore may be more acceptable to patients. Our study used measures to assess and increase the reliability of aural canal thermometry, including checking the visibility of the tympanic membrane via otoscopy, using one outcome assessor, and using an additional measurement of bladder temperature (cited as providing an acceptable near-core measurement). Temperature decline was assessed until the end of the procedure, while other studies also report temperature in PACU (Butwick, et al., 2007). Temperatures measured after arrival in the PACU were not analysed because some patients received postoperative warming interventions; any measurements beyond the arrival temperature into PACU would therefore be confounded.

In conclusion, based on the intention-to-treat results of this study, a short period of preoperative forced air warming, in conjunction with intraoperative IV fluid warming, is not effective at preventing temperature decline in women that receive intrathecal morphine for caesarean delivery. These results do not correspond with the benefits reported for women undergoing caesarean delivery who have received pre-operative warming that continues intraoperatively or have not received intrathecal opioids. However, as intrathecal opioid administration is common practice in many institutions, effective methods of preventing perioperative hypothermia in this population warrant further exploration; combined warming interventions are likely to be of the most benefit.

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6.3 CHAPTER SUMMARY

This study indicates that, while preoperative forced air warming appears to have some benefit, the results are less pronounced than the studies of pre-operative warming where intrathecal opioids have not been administered. The challenges of clinical research and applying rigorous study protocols in a busy clinical environment was also highlighted during the conduct of this study which, in part, contributed to the protocol deviations during the course of the study. However, this also indicated the practicalities and likely clinical issues that would be experienced in implementing this intervention into practice, as well as the likely benefits seen in clinical practice. Nevertheless, as the sample size was inflated to allow for protocol deviations and attrition, the per protocol population represented an adequate sample size as per the power calculation.

When per protocol analysis was conducted (see Appendix T), the results of the pre-operative warming intervention clearly indicated significantly less change from baseline temperature to end of procedure temperature in the intervention group. This degree of change has some clinical significance. The loss of 0.8°C in the control group (versus 0.4°C in the intervention group) is close to the 1.0 °C cited as being the common degree of heat loss experienced in the first hour of anaesthesia (Kurz, 2008) if preventative measures are not taken. This heat loss would have been further pronounced if it were not for the 0.2°C difference between the groups at baseline (where the control group had a higher temperature).

In summary, this study indicates that temperature decline in women receiving intrathecal morphine remains a clinical issue that deserves further investigation. Warming strategies cited as beneficial in other populations may be less so in this population, and careful perioperative thermal care planning is required.

Chapter 7: Discussion

7.1 INTRODUCTION

Perioperative hypothermia is recognised as a significant issue for all patients undergoing surgery. Although awareness of this issue and investigation into effective methods of prevention and treatment has increased in recent years, guidance was still lacking for at least one distinct and vulnerable subgroup of surgical patients, that is, women undergoing caesarean section, leaving a significant gap in literature. The purpose of this multi-phased program of research was to systematically examine the existing evidence for preventing and treating perioperative hypothermia for women undergoing caesarean section, with the view to establishing evidence-based recommendations for practice. The research program also aimed to examine whether special considerations needed to be taken in relation to hypothermia prevention interventions, notably active warming, for this vulnerable surgical population, and whether methods of warming utilised in other populations are suitable and effective for use in women undergoing caesarean section. This chapter will consider the findings from all phases of the research program and aims to situate findings from these studies in the context of current literature.

7.2 THE STATE OF THE SCIENCE

As far as we know, this program of research is the first of its kind to synthesise the current state of the science of hypothermia prevention and treatment specifically targeting women undergoing caesarean section. Internationally accepted guidelines and evidence-based recommendations (Association of Operating Room Nurses ARP Committee, 2007; Hooper, et al., 2010; NCCNSC 2008) have neglected to provide for the obstetric population, leaving health providers who care for women undergoing caesarean section with a lack of clear guidance around the treatment of this condition (Munday, Hines, Wallace, et al., 2013; Petsas, et al., 2009). The potential for the update of the most comprehensive of these guidelines (the NICE guidelines) to incorporate guidance for obstetric patients has been discussed and discounted, as recently as 2015 (National Institute for Health and Care Excellence

2015) despite the first three year review of the guideline in 2011 raising the proposal of widening the scope of the review to include obstetric patients (National Institute for Health and Clinical Excellence November 2011). The reasons behind this have been cited as due to the complex physiological concerns of obstetric patients, which differ to the general population (National Institute for Health and Care Excellence 2015). An additional committee of obstetric experts was considered necessary to oversee this update, but unfortunately it was decided the matter was not a priority (National Institute for Health and Care Excellence 2015).

Concerns regarding the practicality of warming strategies – particularly over body warming blankets – for the awake patient who desires to hold her newborn in the operating room may also have contributed to the decision not to extend recommendations to obstetric patients. It also appears likely that a contributing factor to the lack of guidance for the obstetric population is a lack of importance attached to providing adequate thermal care for this group. This is apparent in the Guideline Development Group's aforementioned assertion that extending guidance to the obstetric population was not a priority (National Institute for Health and Care Excellence 2015), as well as the survey evidence that indicates the lack of attention paid to warming obstetric patients in practice (Woolnough, Hemingway, et al., 2009). In 2010, Chakladar argued that existing recommendations from the 2008 NICE guidelines (NCCNSC 2008) may at least be partly transferable to the caesarean section population, with 'informed interpretation and implementation'[p212] (Chakladar & Harper, 2010). However, this is contrary to the reasons purported for not including obstetric patients in the guidelines - differing and complex physiological concerns of obstetric patients to the general population. Specific guidance for obstetric patients as a distinct group would be valuable, not least because interventions, and strategies deemed suitable and effective for use in the general adult population may not be as effective, and may present challenges in application in this population. Indeed, NICE conceded this by suggesting in 2015 that a guideline to address perioperative hypothermia management for obstetric patients may be considered as part of an extension to a caesarean section guideline (National Institute for Health and Care Excellence 2015) rather than as part of the perioperative hypothermia guidelines for the general adult population (NCCNSC 2008).

As opposed to the general adult population for which guidelines are provided, pregnancy-, surgical- and anaesthetic-related factors, such the vasodilation experienced by pregnant women, the degree of exposure required during caesarean section surgery and the propensity for neuraxial anaesthesia to be used, influence the potential benefits of warming interventions in the obstetric population. Spinal anaesthesia – the anaesthetic mode of choice for the majority of caesarean sections – results in vasodilation in all surgical populations. For women undergoing caesarean section the detrimental thermoregulatory effects of anaesthesia-related thermoregulation may be heightened due to pregnancy related vasodilation, from which decreased vascular resistance also results (Sanghavi & Rutherford, 2014). Vasodilation results in heat being lost from the body's core to the peripheries, and therefore obstetric patients are doubly predisposed to heat loss via vasodilation because of both pregnancy and anaesthetic factors. Women undergoing caesarean section are also inherently disposed to lose heat via body exposure in the operating suite, due to the degree of exposure required to access the surgical site. The centrality of the surgical site to the body also results in limited coverage from upper body coverings and blankets being a possibility, as compared to surgery requiring less exposure, whereby greater body coverage is usually possible. Therefore, reducing convective and evaporative heat loss in caesarean section patients is problematic. Due to the adverse and undesirable side effects of perioperative hypothermia, together with the high reported rates of perioperative hypothermia in this population, (Chakladar, et al., 2011; Hess, et al., 2005) guidance on methods of prevention and/or treatment of this problem is needed. As well as contributing to the generalizability of the systematic review recommendations, the global significance of perioperative hypothermia is illustrated by the geographical spread of the included studies in the systematic review (the United Kingdom, Canada, Iran, the United States, Korea, India, Taiwan and Japan), indicating the scope of the problem internationally.

7.2.1 Updates to the Evidence Base

To consider relevant research that would have met the criteria for potential inclusion in the systematic review and to provide an up-to-date context for this research program, the initial Medline (via EBSCO) search strategy used during the conduct of

the review (in May 2012) was repeated, with the date range of May 2012 to May 2016 (Munday, Hines, Wallace, et al., 2013; Munday, et al., 2014). This further search revealed that four randomised controlled trials specifically testing warming interventions to reduce hypothermia in women undergoing caesarean section have been published since searches were completed for the systematic review (Chakladar, Dixon, Crook, & Harper, 2014; Cobb, et al., 2016 ; de Bernardis, et al., 2015; Paris, Seitz, McElroy, & Regan, 2014). One of these studies (Chakladar, et al., 2014) is not specifically discussed further in this chapter, as the unpublished results were included in the systematic review, however results from the three remaining studies are discussed in the light of the systematic review recommendations. In addition, following the publishing of our systematic review, a meta-analysis of 13 studies investigating the effect of forced air or fluid warming upon maximum maternal temperature change (with secondary outcomes of shivering, thermal comfort, hypothermia, neonatal temperature, umbilical pH and Apgar scores) was also published in 2015 (Sultan, Habib, Cho, & Carvalho, 2015). Findings from this new meta-analysis (Sultan, et al., 2015) are also discussed in context with our systematic review recommendations (Munday, Hines, Wallace, et al., 2013).

7.3 CONTRIBUTING FACTORS TO PERIOPERATIVE HYPOTHERMIA IN WOMEN UNDERGOING CAESAREAN SECTION

While the propensity for obstetric patients to lose heat related to surgical and pregnancy factors has been well documented, this research program also identified and examined other factors related to surgery that influence the development of perioperative hypothermia for caesarean section patients, such as category of surgery, as well as examining the notable influence of anaesthesia and commonly administered medications during caesarean section surgery upon heat loss.

While the predominant focus on the elective caesarean section population could be identified as a limitation of this research program, the retrospective case-control study revealed interesting findings related to the emergency caesarean section patient, establishing that heat loss is a lesser concern for the emergency population of women undergoing spinal anaesthesia, with a statistically significant difference in temperature decline and postoperative hypothermia between the elective and emergency population (see Chapter 5). The lesser incidence of hypothermia may be

partly attributed to the higher incidence of pregnancy-induced hypertension (PIH) in the emergency population, as PIH in itself was found to result in significantly increased temperature, both preoperatively and postoperatively. It seems probable that the vasoconstriction responsible for pregnancy-induced hypertension (Hladunewich, Karumanchi, & Lafayette, 2007) may explain this increase in temperature.

Emergency caesarean section patients are less likely to be waiting for lengthy periods in cool waiting areas prior to surgery. The majority of women undergoing emergency caesarean are likely to have experienced labour, and it has been established that maternal temperature rises with each contraction (Marx & Loew, 1975). It is also widely recognised that some women receiving epidural analgesia during labour experienced fever. The aetiology of epidural analgesia-related fever during labour remains poorly understood (Scott, 2010) but an inflammatory response to epidural anaesthesia remains the most popular theory (Scott, 2010).

Although it seems reasonable to expect that the emergency population is likely to experience higher preoperative temperatures, this was not found to be the case in our study, with similar preoperative temperatures recorded between the emergency and elective groups. The lack of control over the timing of the preoperative measurements in this study should be acknowledged. The emergency group did, however, experience a normothermic mean postoperative temperature of 36.0°C. Nonetheless, a significant proportion of emergency patients (48%) still experienced postoperative hypothermia. Therefore, despite the findings from this study suggesting that preoperative temperature decline is less in this population, clinically significant numbers of emergency caesarean section patients are likely to still experience perioperative hypothermia and thermal care for this group should not be ignored. The challenges of implementing preventative measures in emergency caesarean section are likely to be more pronounced: preoperative warming strategies are less likely to be employed due to the urgency of surgery, therefore the utilisation of appropriate intraoperative warming is especially important. The importance of perioperative temperature monitoring is especially pronounced during emergency caesarean section. Care should be taken to detect not only perioperative hypothermia but also to detect maternal pyrexia, as well as to prevent the inappropriate application

of warming for women who are, in fact, pyrexial or at the upper limits of normothermia.

The difficulties in conducting studies of warming interventions in the emergency population, due to the urgent nature of surgery providing less time for planning of warming interventions and potential recruitment issues, are indicated by the paucity of research examining this area. In total 12 randomised controlled trials were included in the systematic review, but in all but one study (Reidy, et al., 2008) which included 'semi-urgent' cases, participants were undergoing elective surgery.

Most studies included in the systematic review used neuraxial anaesthesia (as spinal or epidural anaesthesia), rather than combined spinal-epidural or general anaesthesia. Phases two and three of the research program were also conducted in the neuraxial anaesthesia population, therefore the results of this research program may not be generalisable to caesarean section surgery under general anaesthesia. This is reflective of practice where neuraxial anaesthesia is generally preferred for caesarean section surgery, both by health care providers and women themselves.

As with general anaesthesia, the potential for medications given during neuraxial anaesthesia to influence both temperature decline, and patient perceptions of temperature, is evident. It is therefore important that warming studies thoroughly report intraoperative medications administered. Some medications particular to caesarean section surgery, such as oxytocin, as discussed by Woolnough et al. (Woolnough, Allam, et al., 2009), have the potential to influence perceptions of warmth. Phenylephrine infusion is commonly administered to patients undergoing caesarean section with neuraxial anaesthesia; it is titrated to blood pressure to prevent hypotension. This approach was utilized during our RCT: however, there are conflicting reports of the effect of vasopressors on perioperative hypothermia. Recent evidence from an observational study suggests that larger doses of phenylephrine result in lower maternal temperatures (although the lowest temperature in this observational study was 36.3°C – well above the hypothermic range) (Hilton et al., 2015). These findings conflict directly with results from an earlier study of patients undergoing elective orthopaedic surgery, where patients receiving phenylephrine (opposed to control) had significantly higher end of procedure temperatures (Ro et al., 2009). Future studies of hypothermia amongst women receiving neuraxial anaesthesia should therefore accurately measure the use and dose of vasopressors,

and other medications such as oxytocics, which may influence maternal perception of heat due to flushing.

While cephalad spread of local anaesthetics during neuraxial anaesthesia have not been intrinsically linked to thermoregulation (Buggy & Crossley, 2000), the influence of administration temperature of local anaesthetic solutions upon shivering (mainly in epidural anaesthesia) has been investigated (Ponte, Collett, & Walmsley, 1986). These studies have considered the influence of cooling upon the extradural space upon the shivering (a heat-generating response), mainly focusing on the efficacy of warming local anaesthetic solutions in epidural anaesthesia (Ponte, et al., 1986). A more recent study by Najafianaraki et al. considered a population of women undergoing elective caesarean section under spinal anaesthesia (Najafianaraki, Mirzaei, Akbari, & Macaire, 2012). In contrast to the epidural anaesthesia studies where warmed versus room temperature local anaesthetics were compared, Najafianaraki et al. compared the effects of cold (4°C) versus 'warmed' (23°C) hyperbaric bupivacaine and fentanyl upon shivering incidence and intensity. It could be argued that the 'warmed' temperature corresponds to what is considered 'room temperature' and that, in practice, cold local anaesthesia and fentanyl is unrealistic as neither drug is required to be refrigerated. The study concluded that the warmer (23°C) solution decreased the incidence and intensity of shivering (Najafianaraki, et al., 2012). Due to the thermoregulatory function of most shivering, as emphasised by Crowley and Buggy (Crowley & Buggy, 2008), if shivering is treated then it is imperative that temperature is also monitored. It also appears reasonable to assert that local anaesthetic and opioid solutions – containing fentanyl and/or morphine - should at least be given at room temperature. The administration of such opioids - integral to neuraxial anaesthesia for caesarean section - is a vital factor when considering perioperative hypothermia aetiology and prevention, and therefore was established as a major focus of this research program.

7.4 INFLUENCE OF INTRATHECAL MORPHINE UPON PERIOPERATIVE HYPOTHERMIA

The role of intrathecal opioids and their potential contribution to maternal heat loss in women receiving neuraxial anaesthesia for caesarean section was evident in the literature and further highlighted by our systematic review findings. The

phenomenon of profound heat loss together with paradoxical symptoms of sweating (as described in Chapter 2) has already been described by numerous authors in case reports (Giladi & Ioscovich, 2015; Hess, et al., 2005; Mach, Van Havel, Gadwood, & Biegner, 2016; Ryan, et al., 2012; Sayyid, et al., 2003; Wishaw, 1997), however the potential differences in effectiveness of warming between differing modes of anaesthesia and administrations of opioids, in 'regular' perioperative hypothermia has also been raised in the literature (Halloran, 2009). In the context of considering the varying results between studies, Halloran raised the question of whether pre-operative warming would be effective where intrathecal morphine had been given (Halloran, 2009). Our systematic review results also reiterated this clinical question (Munday, Hines, Wallace, et al., 2013): however, these results also raised the question of whether there are any differences in temperature decline where intrathecal opioids are given in comparison to non-administration of intrathecal morphine, and the scope of the clinical problem.

Widespread non-administration of intrathecal morphine cannot be expected to be feasible due to the long-lasting, established effectiveness of intrathecal morphine to provide analgesia in this population. Notably, Cobb et al. recognised that a limitation of their recent warming study in this population was the non-utilisation of intrathecal morphine, as this may limit the generalizability of their findings (Cobb, et al., 2016). In addition, although de Bernardis et al.'s recent RCT considering the effectiveness of a pre-operative and intraoperative thermal gown (which was converted to upper body warming during surgery) versus no active warming, did utilise intrathecal morphine, the 80mcg used can be considered to be a low dose, which again may limit the generalizability of their findings (de Bernardis, et al., 2015). Therefore, as well as exploration of the influence of intrathecal morphine upon hypothermia, effective warming for the population of women receiving a clinically commonly given dose of intrathecal morphine needed to be investigated: these needs guided the development of phases two and three of this research program.

The clinical area of the candidate's workplace presented the ideal population to explore the incidence of perioperative hypothermia and temperature decline (phase two of the research program) amongst women who receive intrathecal morphine, in comparison to those who do not receive intrathecal morphine. In this institution, standard anaesthetic practice is to administer intrathecal morphine for postoperative

analgesia during spinal anaesthesia, unless there are contraindications such as allergy, maternal preference or known herpes simplex varus labialis (as intrathecal morphine can reactivate this virus) (Crone et al., 1988). While this study aimed to examine whether there were any differences in temperature decline or hypothermia in relation to administration versus non-administration of intrathecal morphine, a secondary aim was to establish the rate of profound intrathecal morphine related hypothermia (as per Chapters 2 and 5). However, this retrospective case-control study could not establish if there were any differences in effectiveness of warming between women who received intrathecal morphine, and those who did not.

Our retrospective study differed from Hess et al.'s observational study (Hess, et al., 2005) where the incidence of both 'regular' perioperative hypothermia, and profound, prolonged hypothermia, was investigated in 100 patients receiving a dose of 250mcg intrathecal morphine (reported alongside a case series of patients with profound hypothermia). Our study sought to compare perioperative hypothermia amongst both women receiving and not receiving intrathecal morphine in a larger case controlled study, establish temperature decline between these groups, and consider factors that may be associated with perioperative hypothermia.

The low incidence of only 2% of the case-control study population (8/358 patients) experiencing postoperative hypothermia accompanied by sweating, nausea or vomiting, did not enable detailed further investigation of the condition of profound perioperative hypothermia to be conducted. In addition, it was noted that two of these eight patients had not received intrathecal morphine. Given the frequency that the phenomenon is observed to occur in practice, further exploration of this condition could be addressed by conducting a case series of patients experiencing the condition.

Since our observational study was conducted, further case reports of profound hypothermia associated with intrathecal morphine amongst women undergoing caesarean section have been reported (Giladi & Ioscovich, 2015; Mach, et al., 2016), where doses of 150mcg (Giladi & Ioscovich, 2015) and 200mcg (Mach, et al., 2016) have been used. In both cases, the time to the onset of symptoms post spinal anaesthesia was similar and in one study the hypothermia was eventually resolved pharmacologically, via the administration of Naloxone (Mach, et al., 2016). Like earlier authors, both authors of these case reports support the assertion that

intrathecal morphine contributes to cases of hypothermia that are prolonged, characterized by a profound heat loss that is unable to be treated by conventional warming; and the mechanism for this appears to be via alteration of the thermoregulatory centre in the hypothalamus (Giladi & Ioscovich, 2015; Mach, et al., 2016).

It is possible that, despite the findings of our observational study suggesting that temperature decline is similar between women receiving intrathecal morphine and those who do not, that intrathecal morphine does intensify and prolong perioperative hypothermia generally, however in some women the alteration of the set point is markedly greater. In these women the alteration of the sweating, shivering and temperature set points appears to result in the profound and prolonged hypothermia observed in the many case reports described, and in clinical practice. For these women, conventional warming techniques may need to be set aside, as evidence from case reports suggests that pharmacological therapies are effective at resolving the hypothermia. As Mach et al. describe, (Mach, et al., 2016) Naloxone, a μ agonist, has been used to effectively treat the condition in some instances, with small doses being utilized so as to prevent the reversal of the analgesic effects of the morphine (Mach, et al., 2016; Sayyid, et al., 2003; Wishaw, 1997). Benzodiazepines have also been utilised. Midazolam has been reported to be of limited effect due to being short-acting, with symptoms reverting after a period of time (Hess, et al., 2005), whereas Lorazepam is longer acting and there are several reports of this strategy being used to effectively reduce symptoms and assist in resolving the hypothermia, whilst being used with care so as not to result in sedation (Hess, et al., 2005; Ryan, et al., 2012). In the clinical area where the study was conducted, depending on anaesthetic preference, a conservative approach has often been observed with the use of comfort measures to alleviate some of the discomfort from sweating. Once hypothermia is matched by expected symptoms of feeling cold, then warming can be initiated to commence rewarming; however, this can take several hours, during which women have endured significant discomfort and disruption to the post-delivery period, affecting breastfeeding and skin-to-skin.

Although dosage is usually based upon clinician preference, or institutional practices, the optimal dosage of intrathecal morphine has not yet been established (Wong, Carvalho, & Riley, 2013). Lower doses tend to be associated with lesser incidence of

side effects. Girgin et al. found that a dosage of 100mcg, if combined with a low dose of bupivacaine, was comparable with a higher dose of 400mcg in terms of analgesia, but resulted in a lower incidence of itching (pruritus). They also stressed that delayed respiratory depression is less likely with a lower dose (Girgin, Gurbet, Turker, Aksu, & Gulhan, 2008).

Our retrospective, uncontrolled study was able to consider if there were any dose-dependent relationships between morphine and hypothermia, comparing dosages of up to 100mcg with 101-200mcg. No patients received dosages of greater than 200mcg. There were no differences in PACU arrival temperature between these dosage groups, a finding echoed by Giladi et al. (2016) who assert that the severity of hypothermia may not be dose-related (Giladi & Ioscovich, 2015). Based upon literature and practice, Hess et al. used a relatively high dose of 250mcg morphine for all participants (Hess, et al., 2005). It is a possibility that the higher dose of intrathecal morphine used in Hess et al.'s study may have contributed to the 6% rates of profound hypothermia found, although the 32% rate of 'regular' perioperative hypothermia is at the lower end of the scale of published perioperative hypothermia rates in this population (Hess, et al., 2005). Our findings contrast with Hui et al.'s double-blinded RCT where 150mcg intrathecal morphine (compared to saline) resulted in a significantly greater drop in maternal temperature and a longer time to nadir temperature (Hui, et al., 2006), supporting the assertion that intrathecal morphine intensifies maternal temperature decline during spinal anaesthesia. Our study found that increased Body Mass Index, pregnancy-induced hypertension and undergoing emergency surgery were found to result in a decreased likelihood of developing hypothermia, however did not identify any further anaesthetic or surgical factors that may predispose women to develop perioperative hypothermia, or prolonged, profound intrathecal morphine related hypothermia. The findings did indicate that effective warming interventions are needed for all patients, irrespective of whether intrathecal morphine has been administered. The statistically and clinically significant temperature decline across the population found during the retrospective case-control study emphasised the need for further investigation into methods to prevent or minimise heat loss, raising the question as to whether warming strategies should be any less effective where women receive intrathecal morphine.

7.5 INTERVENTION TO PREVENT PERIOPERATIVE HYPOTHERMIA

Strategies included in the systematic review predominantly included IV fluid warming, and/or forced air warming, which are commonly utilised methods of warming across all surgical specialties. Effectiveness is influenced by the timing, duration, temperature setting and method of application of warming and this research program aimed to produce recommendations that were specifically appropriate for caesarean section patients, taking into consideration the varied physiology and issues of practicality already described.

As our review emphasises, warmed IV fluid administration is a feasible and easily applied strategy for reducing maternal temperature decline for women undergoing caesarean section (Munday, Hines, Wallace, et al., 2013; Munday, et al., 2014). Warmed IV fluids are standard care in our institution: therefore results from the retrospective case-control study are reflective of this, and IV fluid warming also comprised standard care during the RCT. It is common practice for caesarean section patients to be administered in excess of 500mls or more, due to the administration of fluid pre-load or co-load to mitigate the vasodilatation and hypotension experienced immediately following neuraxial anaesthesia, together with the operative fluid and blood loss.

In consideration of timing of IV fluid warming, the effectiveness of both preoperative and/or intraoperative IV fluid warming was established by our systematic review with fixed effect meta-analysis indicating IV fluid warming resulted in a higher temperature on arrival to PACU and at 30 minutes after PACU arrival, and a reduced incidence of shivering (see Chapters 3 and 4) (Munday, Hines, Wallace, et al., 2013; Munday, et al., 2014). Methods of warming IV fluids varied, as did the temperature of administration of the fluids, however fluids were analysed as either warmed or unwarmed, with the comparator in these studies commonly cited as 'room temperature' between 20-25°C. Warmed fluids were administered at between 37-42°C, which at the minimum temperature aligns with National Collaborating Centre for Nursing and Supportive Care (NCCNSC) guidance that fluids should be warmed to 37°C for volumes of 500mls or more (NCCNSC 2008).

Differences in the effectiveness of IV fluid warming between studies, and in clinical areas, may be related to the volume of fluids infused, the temperature and timing of administration, but also the solution used. Yokoyama et al. concluded that warmed

(versus room temperature) colloid preload followed by warmed (versus room temperature) crystalloid co-load resulted in a higher maternal tympanic temperature (although it is noted that room temperature was kept to a relatively warm 25°C) (Yokoyama, et al., 2009). It was found that a higher volume of colloid was found to remain in the vascular space, as opposed to crystalloid (Yokoyama, et al., 2009), which could reduce thermal redistribution. Relatively high volumes of fluids (of around 2000mls) during are common during caesarean section surgery, which usually has a surgical duration of less than an hour. Based on the available evidence and the ease of use, it can be asserted that all patients undergoing caesarean section should receive warmed IV fluids as part of standard care. Future guidelines specifically aimed at obstetric patients should accommodate this recommendation, and further consideration can be given to preload with colloid rather than crystalloid solutions.

IV fluid warming, however, may need to be considered as just one aspect of temperature decline prevention, as it may not be sufficient alone. Since publication of our review, a randomised, controlled trial has been published which investigates the effectiveness of a combined warming intervention (IV fluid warming plus intraoperative lower body forced air warming) versus no warming in 46 women undergoing elective caesarean section (Cobb, et al., 2016). This study concluded that the combined warming intervention was effective at decreasing the incidence of hypothermia, however the majority of patients still became hypothermic (Cobb, et al., 2016). Participants receiving the warming intervention had significantly higher temperatures on arrival to PACU, however the mean temperature in both groups was below 36°C. Shivering was not prevented by the warming intervention (Cobb, et al., 2016). Another recently published three-group RCT compared the use of warmed IV fluids versus under body warming (via a warming pad) versus usual care (with room temperature fluids and no warming) in 226 elective caesarean section patients (Paris, et al., 2014), finding that temperatures of patients receiving warmed IV fluids were higher in the operating theatre, however patients with under body warming were the warmest group in PACU.

As with IV fluid warming, timing and duration are also factors pertinent to effectiveness of forced air warming. Systems utilising forced air are commonly available for use with various sizes of blanket, which can be applied either or both

pre-, intra- and postoperatively. Our systematic review was able to recommend the use of preoperative upper body forced air warming, based upon results of narrative analysis, however intraoperative warming alone was not found to be effective, unless combined with preoperative warming. There were some limitations to this analysis: notably the differences in ambient operating room temperature, mode of anaesthesia and opioid administration between studies. In addition, no studies of lower-body warming were considered of sufficient quality for inclusion in the review. Due to the practical difficulties that upper body warming may pose in the operating theatre (restricting the mother's ability to hold her newborn after delivery), and the paucity of lower body warming studies, it was recommended that further intraoperative lower body warming studies were conducted.

The use of under-body warming mattresses was recommended by the review based on a random effects meta-analysis of two studies of maternal temperature on arrival to PACU (Munday, Hines, Wallace, et al., 2013; Munday, et al., 2014). Due to the different modes of under-body warming, further study of the use of these mattresses (carbon polymer versus forced air warming) was also deemed to be necessary for further research. Paris et al.'s recent study of warmed IV fluids versus under-body warming (via a warming pad) versus usual care (with room temperature fluids and no warming) did find that the under-body warming group were the warmest group in PACU (Paris, et al., 2014), however, the incidence of hypothermia, although lower than the other groups, was still high in the under-body warming group. That is, in the operating theatre: 66% in the usual care group versus 38% in the IV fluids group versus 48% in the under-body warming group experienced hypothermia (Paris, et al., 2014). There were some limitations to this study. The randomisation process was unclear, the outcome assessors were not blinded, details of anaesthetic mode or medications were not provided, and it was unclear how long prior to surgery warming interventions were administered nor when observations commenced. Nonetheless, when considered in the light of results from our systematic review, the use of under body mattresses has the potential to reduce practical difficulties that over body interventions may present, whilst applying effective warming to the entire body. This is associated with some benefits that intraoperative over body interventions are not able to achieve. It seems reasonable to assert that warmed body coverings or mattresses should aim for the maximum possible body coverage. It

should also be remembered that perception of warmth below the level of the anaesthetic block is impaired, whilst heat loss remains, therefore patient reporting of warmth below this level should not be relied upon as an indicator of thermal status (Kurz, 2008).

Maximum body coverage should be achievable when utilising preoperative warming. Additionally, the value of preoperative active warming, utilising forced air, in reducing temperature decline is related to the potential to decrease the heat lost via redistribution through the core-periphery gradient by increasing peripheral heat content (Horn, et al., 2002). Recommendations from our review that forced air warming, particularly if applied preoperatively, appears to be effective at improving maternal temperature (although body coverage needs to be considered) are reinforced by the results of Sultan et al.'s recent meta-analysis. This meta-analysis also concluded that warming interventions reduced temperature change (decrease from baseline), resulting in higher end of surgery temperatures and decreased hypothermia (Sultan, et al., 2015). However, there were some differences between the approaches utilised for these systematic reviews, which should be considered. Our review considered different methods of warming separately, however Sultan et al. grouped all studies of different warming interventions together for meta-analysis for the primary outcome of maximum temperature change, and subsequently, significant heterogeneity was found (I^2 = 92%). The authors also stated that publication bias was identified for this primary outcome, based upon the results of Egger's test and funnel plot analysis (Sultan, et al., 2015).

Despite the availability of studies testing preoperative warming for caesarean section, and the recommendations from the systematic review pertaining to preoperative warming, further questions remained as to the effectiveness of preoperative warming for the population of women that receive intrathecal morphine (noted to be related to perioperative hypothermia, as widely discussed). Besides recommending investigation into the influence of anaesthesia mode and intrathecal opioids, upon hypothermia and warming techniques, our systematic review also reiterated that future warming studies use standardized and clinically meaningful temperature measurement time points (Munday, Hines, Wallace, et al., 2013).

At the time of development of the third phase of the research program, there were no published studies investigating the effectiveness of preoperative warming amongst

women that had received intrathecal morphine. Recently, as mentioned earlier, a non-blinded randomised controlled trial has been published that tests preoperative and intraoperative forced air warming amongst women given a small dose of intrathecal morphine (80mcg) (de Bernardis, et al., 2015). However, it is believed that the pragmatic study conducted during this research program is the first to test a short period of forced air pre-operative warming amongst women receiving a clinically common dose of intrathecal morphine. Both groups in our study received IV fluid warming, as per the recommendations from the systematic review (Munday, Hines, Wallace, et al., 2013), standard care in our institution, and existing guidelines for the non-obstetric, adult population (NCCNSC 2008). Therefore, our control group were not completely without any hypothermia prevention strategy, and therefore results between intervention and control groups may not be as marked as in studies where control groups have been completely un-warmed.

Based upon linear mixed model analysis (which allowed for the repeated temperature measurements over time), predicted temperature decline appears to be slower in the preoperative warming group in our study, but not significantly so. This curvi-linear pattern was more pronounced when repeated in per protocol analysis (Appendix T). It appears that a short period of preoperative forced air warming resulted in delaying temperature decline. Patients that received the intervention appeared to experience a plateau in temperature that lasted longer than those who did not receive preoperative warming, before temperature declined to a similar nadir in both groups. De Bernardis et al. also reported the delayed onset of temperature decline in their study of preoperative and intraoperative warming (versus no warming) in women receiving a small dose of intrathecal morphine (de Bernardis, et al., 2015). Significant differences in aural temperature were found between groups, in favour of the intervention group, however the clinical setting for the 60 minute end point is unclear, that is how many patients were in PACU or in the operating theatre at this point, as is surgery duration and anaesthesia time. However, overall they found a statistically significant difference in temperature decline over time between groups. Poor lipid solubility contributes to the slow onset of neuraxial analgesia achieved with morphine (Goma, Flores-Carillo, & Whizar-Lugo, 2014), therefore the possibility of a slower onset of hypothermia, as seen in these studies, should also be considered.

In our RCT, the control group experienced a 0.8°C change from baseline temperature, both during ITT and per-protocol analysis, as opposed to a lower change in temperature in the intervention group (0.5°C in the ITT group versus 0.4°C in the per-protocol group) (Appendix T), which aligns with the theory that while both groups declined in temperature, the decline was more pronounced in the control group. The overall change in de Bernardis et al.'s study cannot be used for comparison, as actual baseline temperature and overall change was not reported (de Bernardis, et al., 2015). The study sample size for our RCT was inflated from the required sample size, based upon power analysis, however utilising a larger sample may have meant that the difference in baseline temperature of 0.2 °C was less significant. In addition, if both groups had commenced at the same baseline temperature, then temperature decline in the control group would have been more pronounced.

Results from ITT analysis in this study may be indicative of results that could be expected to be seen in normal clinical practice, when strict study protocols are not being adhered to; however, in this respect normal clinical practice adjustments would also be possible that may result in greater benefit from warming. For example, the study protocol required 20 minutes of pre-operative warming, and aimed for less than 20 minute delay between the intervention finishing and entry into the OR. This resulted in some protocol deviations, where surgery was delayed due to unforeseen and unpreventable circumstances and a greater than 20 minute delay between warming and entry to the OR ensued. Therefore, in these instances the benefit from the warming intervention was lessened. In normal clinical practice, warming could be extended if similar circumstances arose, therefore maintaining the potential benefit of warming until entry into the OR.

It appears that pre-operative warming in the dose as tested by this study, is insufficient to avoid the development of perioperative hypothermia, but can only delay temperature decline in women receiving intrathecal morphine for caesarean section. A combination approach to warming women receiving intrathecal morphine may be worthy of consideration. Based on the results of their IV fluid warming and intraoperative forced air warming study (versus no active warming) study, Cobb et al. concluded that the recommendations for the use of these modalities proposed by guidelines and regulatory bodies may not be transferable to caesarean section

patients receiving spinal anaesthesia, with only minor benefits expected to be seen (Cobb, et al., 2016). While de Bernardis et al. used a combination approach, intraoperative warming was provided in the form of upper body warming which presents difficulties for mothers when they want to hold their newborns after delivery (de Bernardis, et al., 2015). The use of preoperative forced air warming, IV fluid warming and under-body warming could be explored as a multi-modal approach to preventing the stubborn temperature decline observed in women receiving intrathecal morphine during caesarean section. Preoperative warming may delay temperature decline, while under-body warming could provide an intraoperative mode of warming that can continue during cleaning up time and avoid presenting difficulties for women wanting to hold their babies after delivery.

During the RCT conducted here, it was also observed that the cleaning up time, at the end of the procedure before transfer to PACU, when patients are rolled onto their sides and cleaned, necessitates a large degree of exposure and can result in a temperature drop via radiation before patients reach PACU. It may be that a combination approach, continuing intraoperative warming or use of methods such as under body warming mattresses during the clean-up process, may be of benefit to address this problem. In addition, ensuring the use of warmed fluid used for clean-up may be a simple method to assist in reducing temperature decline lost via convection.

In our RCT, the intervention group commenced at baseline with a 0.2 °C lower temperature than the control group and some patients in both groups could already be considered mildly hypothermic. Therefore, as was emphasized in phase 2 of this research program, results from this randomised controlled trial and other studies, confirm the importance of utilising pre-operative temperature monitoring to identify those patients already thermally compromised, and those at risk. Most caesarean section surgery lasts in excess of 30 minutes duration from incision to clean up. Guidelines for the adult population recommend intraoperative temperature monitoring for surgery expected to be of 30 minutes duration or greater (NCCNSC 2008). Given the duration of caesarean section surgery and the incidence of hypothermia, it seems reasonable to expect that this recommendation can be applied to the obstetric population.

7.6 EFFECT OF WARMING UPON SECONDARY MATERNAL AND NEONATAL OUTCOMES

Varying degrees of benefit have been found from maternal warming upon other maternal and neonatal outcomes, besides maternal temperature. In addition, the issue of whether warming is tolerable to pregnant women is vital to consider: if warming is not acceptable to patients then it cannot be implemented. Tolerability of warming amongst the population is not well reported by studies, however Fallis et al. did report a total of 14/32 patients decreased the temperature of forced air warming in their randomised controlled trial (Fallis, et al., 2006). Overall, warming was found to be well tolerated in our randomised controlled trial, with only one patient ceasing the intervention early (and an additional three patients experiencing a degree of sweating). Therefore, our results indicate that the warming intervention was found to be acceptable to women. During recruitment it appeared that the experience of feeling cold during caesarean section was one that was often remembered by women who had been hypothermic during and after previous caesarean section. Our study did not measure any subjective data regarding temperature and warming, other than maternal thermal comfort, however further qualitative data may be useful in terms of maternal experiences with perioperative hypothermia and the acceptability of warming interventions. There is a paucity of evidence surrounding the experiences of patients in relation to perioperative hypothermia, and the acceptability of warming interventions.

The influence of warming interventions alone upon maternal comfort remains unclear. Narrative analysis from our systematic review found the evidence inconclusive as to the benefit of forced air or IV fluid warming upon maternal comfort (Munday, Hines, Wallace, et al., 2013), while Sultan et al.'s review found warming did improve maternal comfort (however which mode of warming in particular is not clear) (Sultan, et al., 2015). Recently, de Bernardis et al. also found that there was no difference in thermal comfort between women receiving pre-operative and intra-operative warming versus no active warming (de Bernardis, et al., 2015). Our RCT also found no differences in maternal thermal comfort between groups, with no significant difference in ambient temperature between groups (see Chapter 6). As our systematic review discussed, thermal comfort should be considered in relation to ambient operating room and preoperative holding bay

temperature (Munday et al 2013). Studies included in our review indicated that comfort derived from any forced air warming intervention may be greater if ambient temperature is low (Munday, Hines, Wallace, et al., 2013). Our review recommended the maintenance of ambient temperature as an additional strategy to maintain thermal comfort (Munday, Hines, Wallace, et al., 2013). In addition, as found by Fallis et al. (Fallis, et al.), the potential for forced air warmers to increase ambient temperature should also be considered. Future warming studies should also ensure the use of validated scales to measure thermal comfort. Notably, in Cobb et al.'s recent three-group RCT, the authors acknowledged that they used a non-validated thermal comfort scale (Cobb, et al., 2016). As such, as they describe it, the tool appears to measure satisfaction with temperature, rather than thermal comfort itself. As described earlier, the potential for some medications, such as oxytocics, to alter perception of warmth (Woolnough, Allam, et al., 2009) should also be considered when considering thermal comfort scores.

Besides maternal comfort itself, shivering (which commonly causes some discomfort) is commonly included as a secondary outcome or a primary outcome, in warming studies in this population. Intravenous fluid warming and preoperative forced air warming were found to be effective at reducing, what can be considered as presumably thermoregulatory shivering in our systematic review (Munday, Hines, Wallace, et al., 2013), and similarly Sultan et al.'s review found that warming reduced shivering (Sultan, et al., 2015). Although the differences in incidence and intensity of shivering between preoperative warming and usual care groups in our RCT were not statistically significant, there may be limited clinical significance, with 3 patients in the usual care group, versus no patients in preoperative warming group, experiencing shivering assessed as severe.

It should be remembered that shivering is acknowledged as being multi-factorial (Chan, et al., 1989) with thermoregulation responses being only one (but the main) causative factor that contribute to this common, problematic and uncomfortable experience for patients and caregivers. Therefore, while pharmacological therapies were considered for inclusion in our systematic review protocol (Munday, et al., 2012), and pharmacological studies that included maternal temperature as a secondary outcome (and shivering as a primary outcome) were identified, they were excluded from the review itself as the inclusion of these therapies was felt to have

been problematic due to the multi-factorial aspects of shivering. This deviation from the protocol was acknowledged in the published review (Munday, Hines, Wallace, et al., 2013), which also recommended that a further systematic review that focused on pharmacological interventions for shivering might be appropriate, as well as research into the multi-factorial aspects of shivering amongst women undergoing caesarean section. The findings that warming can reduce shivering should therefore be considered in the context of shivering not only being caused by heat loss, as warming may only be able to contribute to at least some decrease in incidence of shivering. Shivering in normothermic patients is often observed in this population, and in these instances, may be considered non-thermoregulatory, but based upon the evidence, it appears that it is reasonable to expect at least some reduction in shivering incidence and severity will result from the application of warming interventions for obstetric patients.

Besides maternal comfort and shivering, related secondary neonatal outcomes of temperature at birth, umbilical pH and Apgar scores have been commonly evaluated in warming studies and were considered during both our systematic review and RCT. Results remain inconclusive, as to the potential direct benefit these neonatal outcomes may receive from maternal warming. No conclusive benefits were found from warming upon neonatal outcomes in our systematic review (Munday, Hines, Wallace, et al., 2013), and the preoperative warming intervention tested in the RCT did not result in any significant difference in median neonatal temperature or Apgar score between groups. The RCT found only a 0.2°C difference in median neonatal temperature in favour of babies born to mothers who had received preoperative warming, with the median temperature in both groups within the normothermic range for neonates. Sultan et al. found that umbilical pH was improved in babies born to mothers who had received warming but Apgar scores were not altered by warming (Sultan, et al., 2015). Similarly, Cobb et al. also found no significant differences in Apgar score or umbilical vein blood gases (Cobb, et al., 2016). Despite the lack of direct benefit upon neonatal outcomes, it is likely that benefit is derived from preventing hypothermia in mothers, which can enable earlier breastfeeding and bonding to occur, as indicated from the greater proportion of participants in the preoperative warming group that achieved skin-to-skin contact of over 30 minutes during our RCT.

Therefore, it can be asserted that overall results conflict (based upon this RCT, the systematic review and recent published literature) as to whether maternal warming can improve neonatal outcomes (Munday, Hines, Wallace, et al., 2013), but also that further research of the potential effect of maternal warming and environmental operating theatre factors upon neonatal outcomes is warranted. A recent study evaluated the impact of ambient OR temperature upon neonatal temperature (and maternal temperature), suggesting that an increase to 23°C (versus a cool 20°C) decreased neonatal hypothermia (Duryea et al., 2016). The influence of external, environmental factors upon neonatal hypothermia such as ambient temperature and skin-to-skin contact at birth should be considered further to improve thermoregulatory care of the newborn after caesarean section.

7.7 CHALLENGES TO IMPLEMENTING THERMAL CARE RECOMMENDATIONS FOR OBSTETRIC PATIENTS

Our systematic review was used as the basis for a JBI Best Practice Information Sheet (Giles, et al., 2013), which therefore contributed in part to the fulfilment of the aim to formulate up-to-date and specific recommendations for temperature management in women undergoing caesarean section. The retrospective case-control study highlighted the lack of consistent documentation for temperature monitoring and treatment and the greater concern for elective caesarean section hypothermia prevention versus emergency surgery. It appears reasonable to assert that elective surgery pathways should therefore employ consistent temperature monitoring, pre-emptive methods of preventing temperature decline and safeguards to ensure these strategies are recorded.

The potential challenges of applying the above and other recommendations related to perioperative thermal care into anaesthetic practice should not be underestimated. As Levin et al. emphasise evidence-based changes to perioperative practices require partnership between the many professional groups that are involved in the perioperative suite if they are to achieve sustainability (Levin, Wright, Pecoraro, & Kopec, 2016). The challenges of involving such large groups of staff have been recognized by the candidate as a practice implementation barrier in an earlier evidence-based practice implementation project (Munday, Hines, & Chang, 2013). Gaining consensus is vital to the success of implementation change and the early

involvement of stakeholders is viewed as a facilitator to effective practice change (Levin, et al., 2016; Munday, Hines, & Chang, 2013). Potential barriers may also arise from the hierarchical structure that is evident within the perioperative environment and a practice change that is nurse-led but impacts directly upon anaesthetic practice may experience resistance. Therefore, the benefit to establishing a multidisciplinary team, specifically including anaesthetic staff and also surgical staff, to lead the evidence-based practice change cannot be underestimated. This approach can also be a facilitator to the successful conduct of primary research in the perioperative environment, and indeed the involvement of anaesthetic personnel in the research team for the RCT conducted during this research program was considered to be instrumental in easing the conduct of the RCT. Also found to be vital was the careful consultation of all involved parties in the planning and preparation stages of the RCT before recruitment and data collection commenced. Similar approaches as used during the conduct of the RCT, can therefore considered as worthy of consideration during the stage of practice change implementation.

7.8 CHALLENGES TO PRAGMATIC CLINICAL RESEARCH IN VULNERABLE POPULATIONS

Widespread consultation and communication is also pertinent in the context of ethical approvals for planned research. Careful consideration was taken regarding the potential ethical issues of conducting experimental research upon pregnant women during the planning stages of the RCT. Pre-emptive communication and advice from the hospital human research ethics committee office, prior to submitting the application, also facilitated the process of ethical approval by ensuring that relevant issues were considered in depth during the application development. The application was also developed with reference to the National Statement on Ethical Conduct in Human Research 2007 (updated 2015), acknowledging section 4.1.1 that 'the wellbeing and care of the woman and of her fetus always takes precedence over research considerations'[p47] (National Health and Medical Research Council , Australian Research Council , & Australian Vice-Chancellor's Committee 2007)(p47), as well as the implication that by participating in the research women also involved their unborn baby (as per the National Statement 4.1.4) (National Health and Medical Research Council , et al., 2007). Particular attention was given to the

potential risk of overheating by preoperative warming for both mother and baby. This was reflected in the exclusion criteria stipulating that any participant with a preoperative baseline temperature of >37.0°C was excluded. Such considerations are considered pertinent to future warming studies conducted in the obstetric population.

7.9 LIMITATIONS

While the systematic review did not specifically exclude studies including women undergoing emergency caesarean section, as previously mentioned only one included study (Reidy, et al., 2008) included both elective and 'semi-urgent' cases. Therefore, there may be limited generalisability of the recommendations to emergency caesarean section surgery. In addition, the randomised controlled trial included only patients undergoing elective surgery. Although potentially problematic to undertake, further research may be needed because the urgent nature of emergency caesarean section may render preoperative warming interventions that require forward planning and adequate time to implement prior to surgery unachievable: however, as discussed earlier, findings from the retrospective case-control study did indicate that the population of women undergoing emergency caesarean section experienced significantly less heat loss.

Furthermore, phases two and three of this research program focus upon the population of women receiving spinal, rather than epidural anaesthesia, which could be considered to limit the generalisability of the overall research findings. The systematic review did include studies where either mode of anaesthesia was utilised.

Meta-analysis was inhibited in the systematic review due to the clinical heterogeneity of the included studies in the systematic review; therefore, only a few meta-analyses were undertaken. There were many variations in temperature outcomes related to time-points, particularly intraoperatively. Mode of temperature measurement was not specified in the inclusion criteria for the systematic review, however the use of a consistent method of measurement with studies was considered vital (Munday, Hines, Wallace, et al., 2013). Variation in reliability between temperature measurement methods is a well-recognised limitation in studies of temperature and warming. The randomised controlled trial aimed to use temperature measurement time points that would be clinically useful, and also aid comparability with other

published research. Nonetheless, the potential limitations of aural canal thermometers are also recognised. Therefore, measures to partially address these issues were implemented. Firstly, one operator used one calibrated device for the entirety of the study. Secondly, the exclusion criteria allowed for the exclusion of patients if, upon otoscopy, the tympanic membrane was not visible, including if this was due to earwax. Thirdly, intraoperative bladder temperatures, considered to represent near-core temperature, were utilised as a secondary measure of temperature measurement and Bland-Altman analysis was undertaken to measure agreement between these two routes.

Data collection for the retrospective case-control study was subject to the problems inherent in utilising pre-collected data from patient charts. While data collection in this manner is problematic, due to missing data and because the data collected was not collected for the primary aim of research, there are further challenges in relation to collecting temperature data via this method. Firstly, the importance attached to the monitoring and recording of temperature within the perioperative department both in the practice area (and internationally) appears to be low (Arkilic, et al., 2000). Secondly, the reliability of temperature monitoring devices used over the study period cannot be assured, nor can consistent practice between operators. It is well known that some methods of temperature measurement, including the aural canal measurements used in the practice area, are particularly vulnerable to operator inefficiency. Thirdly, there is a limited ability to control for confounding factors influencing temperature; ambient temperature is not recorded in patient health records and warming strategies may not be thoroughly documented. It should be noted that, according to Australian College of Operating Room Nurses (ACORN) Standards for Perioperative Nurses in Australia, ambient OR temperature is required to be maintained within a specific range of 20-22°C, (Australian College of Operating Room Nurses 2012.), however waiting and postoperative areas may have more variance.

Due to incomplete documentation in patient charts, the retrospective case-control study lacked data on intraoperative temperature and warming, and therefore postoperative hypothermia on arrival to PACU was used as an indicator for intraoperative temperature decline. To address this, the randomised controlled study collected and used intraoperative data to the end of procedure as an indicator of

intraoperative temperature decline rather than postoperative data from PACU. This was due to the necessary variations in practice and the requirement to implement further warming on an individualised basis, prior to breastfeeding, in PACU, which would have resulted in confounding if this data had been included in further analyses.

The existence of protocol deviations during the conduct of the RCT could be considered as a limitation of this study: however, the sample size was inflated to allow for protocol deviations in view of the anticipated challenges of conducting the study in the busy clinical setting. The conduct of research requiring adherence to strict study protocols in clinical environments presents challenges, which cannot be underestimated or, in some cases, planned for. Anticipated situations that would require deviation from the study protocol were considered during the development of the study, particularly related to the exclusion criteria and protocol (such as extended time between preoperative warming and entry to the operating theatre). The widespread education of staff in all areas affected by the study was undertaken to reduce protocol deviations due to staff not understanding, or not being aware of the study aims and protocol. To this end, gaining agreement and consensus between key personnel and managers during the planning stages of the study was also vital. Some situations that occur in a fast-paced, tertiary clinical environment, such as the perioperative department where the RCT was conducted, cannot be anticipated. The protocol deviations related to suspected bladder injury requiring blue dye and bladder irrigation invalidated the bladder temperature measurements in those three cases: such instances are unexpected and generally rare.

Despite the challenges of conducting research in the clinical setting, the benefits of using a pragmatic trial approach are evident. The RCT was aimed to test an intervention that could, if effective, be integrated into existing care pathways with minimal disruption. Such a pragmatic approach also promotes the generalisability of the findings and provides an indication to how the intervention may work in real-life clinical practice (Patsopoulos, 2011), and such studies may be more valuable to those responsible for developing policy (Patsopoulos, 2011; Ware & Hamel, 2011). Our study indicates that this intervention can be feasibly integrated into similar existing care pathways: outside of a research setting, the benefits of the preoperative warming may actually be maximised as necessary alterations can be made and the strict study

limits (for example, in relation to maximum time between warming and entry to the operating theatre) can be adjusted for maximum benefit (as discussed in Chapter 6).

7.10 SUMMARY

The challenge of maintaining temperature and reducing heat loss in this population remains. Based upon this program of research, some recommendations formulated for the general adult population (NCCNSC 2008) can be applied to the obstetric population: namely, that pre-operative and intraoperative temperature monitoring should occur, and that IV fluid warming should be instigated. However, whilst some clear benefit is derived from IV fluid warming, pre-operative warming and intra-operative warming in terms of reducing maternal temperature decline and shivering, any of these interventions alone is insufficient to prevent the significant temperature decline that the majority of caesarean section patients are vulnerable to, due to neuraxial anaesthesia itself, and the use of intrathecal morphine which contributes to intensify temperature decline. Conventional warming methods are also not effective in the small subset of women that experience the less common, but particularly problematic and uncomfortable, severe and prolonged temperature decline attributed to the cephalic spread of morphine altering the temperature set point. For these women, pharmacological therapy appears to reverse the hypothermia, but needs to be used with care. Warming appears to be well tolerated in this population, and a combination approach to warming incorporating pre-operative and intra-operative strategies with careful temperature monitoring should be considered.

Chapter 8: Conclusion

8.1 INTRODUCTION

Inadvertent perioperative hypothermia is a significant adverse event for women undergoing caesarean section surgery, associated with numerous unwanted side effects for women as well as increased healthcare costs, prolonged stay and significant disruption to the surgical pathway. Yet, recommendations to guide health care providers to decrease the incidence of this condition have been absent. The studies presented here are believed to represent the first comprehensive three-phased research program that seek to provide guidance for perioperative hypothermia prevention specifically for obstetric patients. This chapter presents the implications for practice and future research arising from the findings of this research program.

8.2 IMPLICATIONS FOR PRACTICE

This research program has resulted in specific recommendations, previously lacking and clearly needed, for the thermal care of women undergoing caesarean section, as well as highlighting areas for future research. These recommendations reflect the need for proactive, evidence-based thermal management to prevent perioperative maternal temperature decline and to reduce the incidence of perioperative hypothermia, enhancing and improving the perioperative care provided to women undergoing caesarean section for delivery of their babies.

Recommendations for practice that are supported by this research program are detailed below and presented in order of importance:

1. Firstly, regular and timely assessment and documentation of preoperative, intraoperative, and postoperative maternal temperature should be integrated into routine practice. Regular and timely assessment of maternal temperature enables effective care planning aimed at not only preventing temperature decline and reducing risk of hypothermia but also early detection of hypothermia and timely intervention to reduce further temperature decline and restore normothermia.

To facilitate this, temperature monitoring devices need to be readily available, and perioperative documentation (such as preoperative checklists) should clearly allow for the recording of preoperative and intraoperative temperature.

2. Combined, multi-modal, warming strategies should be considered in the place of single interventions for all women undergoing caesarean section, as appropriate and with consideration to maternal temperature readings, to ensure warming is instigated where appropriate. These strategies should include: warmed IV fluid preload and intraoperative IV fluid warming, preoperative forced air warming and active intraoperative warming which may include over body forced air or under body warming mattresses.

3. Health care providers should be cognisant of the exacerbation of temperature loss and decreased ability of warming to prevent hypothermia, in settings where intrathecal morphine administration is routine. In these settings, it is imperative that monitoring of temperature, in conjunction with preoperative and intraoperative warming interventions, form standard care and that this is reflected in hospital policies.

4. Maintenance of ambient temperature within existing guidelines for OR ambient temperature, – such as the ACORN Standards in Australia (Australian College of Operating Room Nurses 2012.) - should be used to maintain thermal comfort and a protective thermal environment for both mothers and neonates.

6. Health care organisations should develop evidence-based thermal care guidelines that incorporate strategies with demonstrated effectiveness in reducing risk for perioperative hypothermia specifically for the perioperative care of obstetric patients. Guidelines should consider and specifically address such needs as unique changes in physiology, anaesthetic risk factors, maternal comfort, challenges in implementing hypothermia prevention strategies, and the influence of intrathecal opioids upon temperature decline and the effectiveness of warming. In conjunction with the guidelines, evidence-based, useable clinician tools should be developed and promoted for use by medical, nursing and ancillary staff, to reduce the incidence of perioperative hypothermia in this vulnerable population. Specifically, clinical tools related to temperature monitoring are required that promote timely preoperative, intraoperative and postoperative monitoring. Clinical algorithms that direct the appropriate use of warming, as indicated by preoperative temperature status, and

planned intrathecal opioid use, should be available for use for clinicians caring for women undergoing caesarean section, such the tools developed by NICE for use in adult surgical populations (NCCNSC 2008).

7. Education of perioperative and anaesthetic staff should reinforce the importance of avoiding perioperative hypothermia, emphasise the necessity to consistently monitor maternal perioperative temperature and equip staff with the knowledge of appropriate warming strategies. Staff should also be educated regarding the use of clinical algorithms, where developed, that aid decision-making regarding appropriate thermal care for women undergoing caesarean section.

8.3 FUTURE RESEARCH

This research program provides evidence that is predominantly relevant to elective, rather than emergency caesarean section surgery. Therefore, further research into the effectiveness of warming interventions, which also considers the feasibility of these interventions for emergency caesarean section is warranted. In addition, given that most caesarean section surgery is undertaken on awake patients under neuraxial anaesthesia, the perspectives of women regarding warming interventions, particularly acceptability, would be worthy of exploration. Finally, further work is needed to identify factors that may contribute to prolonged intrathecal morphine related hypothermia, to optimise appropriate perioperative care planning and risk management.

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Appendix A

The clinical effectiveness of interventions to assist perioperative temperature management for women undergoing caesarean section: a systematic review.

Executive summary

Background

Women undergoing caesarean sections are vulnerable to the adverse effects associated with inadvertent perioperative hypothermia. Effective methods for preventing or managing hypothermia in this group would be valuable.

Objectives

To synthesize the best available evidence in relation to preventing and/or treating hypothermia in mothers after caesarean sections.

Inclusion criteria

Types of participants

Adult patients of any ethnic background, with or without co-morbidities, undergoing any mode of anaesthesia for any type of caesarean section were included.

Types of interventions

Active or passive warming methods, versus usual care or placebo, that aim to limit or manage core heat loss as applied to women undergoing caesarean sections are included.

Types of studies

Randomised controlled trials that met the inclusion criteria were considered.

Types of outcomes

Primary outcome: maternal core temperature during preoperative, intraoperative and postoperative phases of care.

Secondary outcomes: newborn core temperature at birth, umbilical pH measured via blood gas analysis, Apgar scores, length of Post Anaesthetic Care Unit stay, maternal thermal comfort.

Search strategy

A comprehensive search was undertaken of the following databases from their inception until May 2012: ProQuest, Web of Science, Scopus, Dissertation and Theses PQDT (via ProQuest), Current Contents, CENTRAL, MedNar, OpenGrey and Clinical Trials. There were no language restrictions.

Methodological quality

Retrieved papers were assessed for methodological quality by two independent reviewers using the standardized critical appraisal instruments for randomised controlled trials from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instruments (JBI-MAStARI).

Data collection

Two independent reviewers extracted data from the included papers using a customized data extraction tool.

Data synthesis

Where meta-analysis was possible, results were combined in a fixed effects meta-analysis using the Cochrane Collaboration Review Manager software. Due to heterogeneity for one comparison/outcome, random effects meta-analysis was also used.

Results

Twelve studies with a combined total of 719 participants were included. Intravenous fluid warming was found to be effective at maintaining maternal temperature and also aided in shivering prevention. Intravenous fluids did not improve thermal comfort or neonatal temperature, and the effectiveness on Apgar scores and umbilical pH remains unclear.

Warming devices, including forced air warming devices and under-body carbon polymer mattresses, were effective at preventing hypothermia; however effectiveness increased if applied preoperatively. Preoperative body warming devices also reduced shivering. Preoperative forced air warming improves neonatal temperatures. Forced air warming did not improve Apgar scores. The effectiveness of body warming devices on umbilical pH and thermal comfort remains unclear.

Leg wrapping was not effective for maintaining maternal temperature.

Conclusions

Intravenous fluid warming, by any method, improves maternal temperature for women undergoing caesarean section and reduces shivering. Preoperative body warming devices also improve maternal temperature, in addition to reducing shivering.

Implications for practice

Preoperative warming strategies should be utilized where possible for women undergoing caesarean section (Level 2) and preoperative and/or intraoperative warmed IV fluids should be standard practice (Level 1).

Under-body warming mattresses should be used (Level 1) and upper body forced air warming should be utilized preoperatively (Level 2).

Additional strategies, such as ambient temperature maintenance, should be used to maintain thermal comfort (Level 2). Warming strategies have less effect when intrathecal opioids are administered (Level 2).

Implications for research

Research is needed to investigate the effectiveness of interventions in emergency caesarean section surgery. Larger scale studies of warming interventions using standardized and clinically meaningful temperature measurement time points are also required.

Keywords

perioperative, hypothermia, caesarean section, warming, systematic review

Introduction

Background

Women undergoing caesarean section (CS) are vulnerable to the adverse effects associated with perioperative core temperature drop during surgery, in part due to the tendency for this surgery to be performed under neuraxial anaesthesia, and due to higher rates of blood and fluid loss. Vasodilation, which occurs in all pregnant patients, also predisposes obstetric patients (Dunn, et al., 1993) to inadvertent perioperative hypothermia (IPH).

IPH is a common condition that affects patients undergoing surgery of all surgical specialties and is detrimental to all age groups, including neonates. Numerous serious adverse effects are associated with IPH for all patient groups. Increased blood loss and transfusion requirements (Rajagopalan, et al., 2008) stem from impaired platelet function in hypothermic patients. Even in this respect alone, the prevention of hypothermia would be particularly beneficial for caesarean section patients, for whom perioperative bleeding can present significant problems (Woolnough, Allam, et al., 2009). Delayed wound healing (Kurz, et al., 1996), decreased immune response (Beilin, et al., 1998) leading to increased wound infection rates (NCCNSC 2008), prolonged stay in Post Anaesthetic Care Units (PACU), prolonged hospital stay and increased costs (Lenhardt, et al., 1997), altered drug metabolism and increased likelihood of cardiac arrhythmias (NCCNSC 2008) have also been associated with IPH, and this list may not be exhaustive. Shivering associated with hypothermia also places patients under increased cardiac strain.

In the early 1990s, maternal hypothermia was described as being rarely discussed in obstetric literature (Dunn, et al., 1993) but in recent years studies have scrutinized methods of preventing hypothermia specifically for this group of patients. Also, in recent years, multiple systematic reviews and guidelines have been published with the aim to provide evidence for the effective prevention and management of IPH. These largely focus on either adult or all ages' populations, but have mainly overlooked, or excluded, pregnant or CS patients as a distinct and vulnerable group. A JBI systematic review on the management of perioperative hypothermia included three studies that focused on the warming of CS patients (and identified no other studies of CS warming in excluded articles), (Moola & Lockwood, 2011) with searches complete to 2008. A meta-analysis on cutaneous warming systems (Galvao, et al., 2010) included two studies that pertain to the warming of CS patients. While the National Institute for Health and Care Excellence (NICE) guidelines (2008) (NCCNSC 2008) on IPH excluded pregnant women, Chakladar & Harper suggest that guidelines and clear evidence are needed to establish what constitutes best practice in terms of preventing IPH in this group of patients (Chakladar & Harper, 2010).

In addition, not all recommendations made by systematic reviews targeting all adult patients are readily transferable to CS patients. Practical problems may exist with using forced air warming for obstetric patients.(Chakladar & Harper, 2010) (Petsas, et al., 2009) Forced air warming blankets (the warming mode of choice recommended by NICE (NCCNSC 2008)) have been described as difficult to apply in such a way that they do not interfere with the mother and baby.(Chakladar, et al., 2011) Obstetric patients may also have different thermoregulatory responses in comparison to non-pregnant controls (Liu & Luxton, 1991) which may affect the effectiveness and appropriateness of warming devices. The vasodilation experienced by all pregnant patients is exacerbated by neuraxial anaesthesia, thus increasing heat loss. Oxytocics also produce vasodilation thus increasing heat loss. CS patients may also be particularly vulnerable to hypothermia due to the amount of exposure required during surgery and the large amount of fluid loss experienced, in particular during emergency surgery. Hypothermia is usually initially undetected during neuraxial anaesthesia (commonly used for CS). This occurs if the temperature is not monitored by the anaesthetist during neuraxial anaesthesia (Arkilic, et al., 2000;

Lenhardt, et al., 1997). In addition, behavioural thermoregulation is impaired. Patients may not perceive and therefore report that they are cold (Arkilic, et al., 2000).

Skin surface heat loss occurs via the four mechanisms of radiation, convection, evaporation and conduction (Dunn, et al., 1993) – all of these mechanisms combine during surgery to produce a problematic heat loss which can result in hypothermia. Environmental factors, such as the ambient temperature of the operating theatre and downward draft, result in convective and radiant heat loss, when large areas of the skin's surface are exposed to the relatively cool surrounding environment. Wet linen, room temperature irrigating fluids and skin cleansing fluids contribute to conductive and evaporative heat loss (Dunn, et al., 1993). The duration of the surgery, and systemic and neuraxial medications also contribute to the overall likelihood or extent to which hypothermia will develop.

It has been suggested that all CS patients should receive intraoperative warming, (Harper & Alexander, 2006) because if it is not managed, the rate of hypothermia in patients undergoing spinal anaesthesia for CS could be as high as 80% (Harper & Alexander, 2006). During spinal anaesthesia, as in general anaesthesia, heat redistributes down a core-periphery heat gradient. Heat is therefore redistributed from the core compartment to the peripheries due to the vasodilation caused by the sympathetic block. (Sayyid, et al., 2003) Secondly, below the level of the block there is a loss of thermoregulatory vasoconstriction (Sayyid, et al., 2003), and, thirdly, thermoregulation impairment results in reduced thresholds for shivering and vasoconstriction during spinal anaesthesia (Sayyid, et al., 2003).

The effects of certain drugs used during spinal anaesthesia, notably intrathecal morphine, may also exacerbate IPH. Morphine is commonly used in spinal anaesthesia for CS to give a longer duration of postoperative pain relief, but is known to be associated with hypothermia, even in small amounts (Hui, et al., 2006). It is thought that the drug spreads in the cerebrospinal fluid to the body's thermoregulation control centre – the hypothalamus – and impairs thermoregulation (Hui, et al., 2006). The paradoxical symptoms that sometimes occur with hypothermia associated with intrathecal morphine have been attributed to the decrease in the thermoregulatory set point that is believed to occur due to the cephalic spread of the opioid. In these patients, paradoxical symptoms of feeling hot

combined with diaphoresis alongside hypothermia have been observed (Hess, et al., 2005). Active warming may not be tolerable for patients experiencing these paradoxical symptoms, although they are hypothermic. Maintenance of normothermia in patients given intrathecal morphine therefore presents a greater challenge and it may be that warming methods that are effective for other patients may have a reduced effect or appropriateness in this group of patients. Alternative, effective methods for preventing or managing hypothermia in this group would therefore be valuable.

In all obstetric patients, the temperature status of the mother and the unborn baby are related. A temperature gradient exists between the warmer unborn baby and the cooler mother (Yentur et al., 2009). Babies born to hypothermic mothers may also be at risk of lower temperatures at birth and possibly lower umbilical pH and Apgar scores at birth (Horn, et al., 2002; Petsas, et al., 2009).

Warming interventions are usually classified into two groups, according to the means of transferring heat. Passive warming measures warm the peripheries or skin surface and include reflective (space) blankets, cotton blankets and other types of coverings. Active warming measures aim to increase the core heat content, and employ convective means of heating. Forced air warming devices, circulating water garments, heated mattresses and intravenous fluid warmers are all examples of active warming measures. Active warming – forced air warming blankets in particular – is the recommended means of preventing and managing IPH according to evidence-based guidelines published by NICE (NCCNSC 2008) and by the JBI systematic review on IPH (Moola & Lockwood, 2011). Circulating water garments have also shown potential to be at least as effective, if not more effective, as forced air warming blankets, according to a recent meta-analysis (Galvao, et al., 2010). Prewarming patients prior to surgery, usually via active warming methods, has been recommended (NCCNSC 2008) to decrease the redistribution of heat occurring during the first phase of anaesthesia by increasing the peripheral heat content. These interventions may have varying degrees of usefulness, effectiveness and applicability for CS patients. Any risks associated with using warming interventions may also be magnified for pregnant patients, for example, maternal overheating or high maternal body temperature may adversely affect fetal wellbeing (Lieberman et al., 2000).

Apart from the undesirable physiological adverse side effects associated with IPH, the condition can also have the potential to adversely affect maternal experiences in, and satisfaction with, the Recovery Unit phase. Discomfort and shivering, both side effects of IPH, can create problems during the postoperative period (Butwick, et al., 2007) which may interfere with the mother's ability to be with and bond with her newborn, at a time when breastfeeding is often instigated.

As indicated above, no other systematic reviews have been published that deal exclusively with the effectiveness of warming methods for patients undergoing CS. Recommended methods of warming other patient groups may have differing levels of effectiveness, applicability and practicality for this population. This review aims to address the lack of existing guidance by providing recommendations specifically for women undergoing CS.

Objectives

This systematic review sought to synthesize the best available evidence in relation to preventing and/or treating hypothermia in mothers after CS surgery.

More specifically, the objective was to synthesize the best available evidence on the effectiveness of interventions to prevent heat loss in this group of patients. This included active warming measures (such as forced air warming and intravenous [IV] fluid warming) or passive warming measures (such as leg wrapping and prewarming), on the core temperature of the mother and newborn after surgery.

Review questions

- What are the most effective interventions for preventing and managing perioperative hypothermia in women undergoing CS surgery?
- Are there any differences in effectiveness for warming interventions between patients undergoing different modes of anaesthesia for CS (general /epidural/spinal)?

Definitions

Hypothermia: a patient core temperature of below 36°C (NCCNSC 2008).

Normothermia: a core temperature between 36°C and 38°C (Hooper, et al., 2010).

Gravida: number of pregnancies (Johnson, 2010).

Parity: the number of previous deliveries (Kenner & Lott, 2007).

Neuraxial: spinal or epidural anaesthesia (Arkilic, et al., 2000).

Active warming: methods that minimize convective heat loss (Torossian, 2008), for example, forced air warming, circulating water garments and fluid warming devices.

Passive warming: methods that warm the patient by minimizing heat dispersion and insulating the patient from the environment (Putzu, Casati, Berti, Pagliarini, & Farelli, 2007), for example, cotton blankets and aluminium foil covers.

Inclusion criteria

Types of participants

All studies of adult patients over the age of 18 years, of any ethnic background, with or without co-morbidities, undergoing any of the different modes of anaesthesia (general/epidural /spinal) for any type of CS (emergency or planned) at healthcare facilities who have received interventions that may limit or manage perioperative core heat loss were included. Studies focusing on patients undergoing any other type of surgery other than CS or pregnant patients not undergoing CS were excluded.

Types of interventions

The types of intervention considered were: active warming methods or passive warming methods versus usual care or placebo, that aim to limit or manage core heat loss as applied to women undergoing CS. Active warming methods include forced air warming devices, warmed fluids, warmed mattresses and warmed coverings. Passive interventions include unheated coverings, such as leg wrapping.

Types of studies

This review considered any randomised controlled trials (RCTs) that met the inclusion criteria, with reduction of perioperative hypothermia a primary or secondary outcome.

Types of outcomes

The review focused on the following outcomes:

Primary outcome: maternal core temperature measured via the following sites: pulmonary artery, oesophageal, tympanic, bladder or oral, during the preoperative, intraoperative and postoperative phases of care.

Secondary outcomes: newborn core temperature at birth obtained immediately after birth, umbilical pH measured via blood gas analysis from a sample obtained immediately after birth, Apgar scores, length of Post Anaesthetic Care Unit (PACU) stay measured in minutes from the time the patient arrives into PACU until discharge to ward areas, and maternal thermal comfort (preferably measured by a validated scale).

Search strategy

The search strategy incorporated both published and unpublished literature, including grey literature, in any language. A three-step search strategy was utilized. An initial limited search of Medline, CINAHL and EMBASE was conducted, followed by an analysis of the text words contained in the title and abstract, and the index terms used to describe the article. A second search included all identified keywords and index terms across all databases listed. Thirdly, the reference lists of all identified studies and articles were hand searched. The date range for searches was from the inception of the databases until May 2012.

Additional databases searched:

ProQuest

Web of Science

Scopus

Dissertation and Theses PQDT (via ProQuest)

Current Contents

CENTRAL

MedNar

OpenGrey

Clinical Trials

All studies identified during the database search were assessed for relevance to the review based on information via the title, abstract and description by two independent reviewers. A third reviewer was consulted if consensus could be reached. The full article was retrieved for all those that appeared to meet the inclusion criteria. Any articles that appeared unclear in this respect were also retrieved for clarification. Details of search terms used are detailed in Appendix C. Search results are detailed in Appendix D.

Initial keywords

perioperative or peri-operative or intra-operative

surgical

temperature OR core temperature

thermoregulation

hypothermia

shivering

C*esarean section

C*esarean delivery

parturient

maternal

warming

active warming

passive warming

Verification of relevance

All studies were assessed for relevance to the inclusion criteria using a form developed by the reviewers and based on the recommendations of the Cochrane Collaboration (Deeks, et al., 2011) (Appendix E).

Method of the review

Assessment of methodological quality

Papers selected for retrieval were assessed for methodological quality by two independent reviewers (JM, SH) prior for inclusion in the review using the standardized critical appraisal instrument for RCTs (Appendix B) from JBI-MAStARI. Disagreements regarding three papers were resolved via consultation with the third reviewer (KW).

In addition, an assessment of quality of the included papers was made in relation to five key quality factors. Studies were stratified as low, medium or high quality according to how these factors were addressed in each included study. Description of the random assignment to treatment groups was examined, as were details of participant blinding to treatment allocation, the concealment of allocation to treatment groups to allocator, the description and inclusion in the analysis of those participants who withdrew, and the blinding of outcome assessors.

Data collection

Two independent reviewers (JM, SH), extracted data from the included papers using a customized data extraction tool, based on the JBI data extraction tool for quantitative studies. This tool was piloted by two of the reviewers (JM, SH) extracting data from the same study during protocol development, prior to use with

the included studies (Appendix F). The extracted data included details of the intervention, population, study design, outcomes and data relevant to the review question and objectives.

Data analysis

Where meta-analysis was possible, results were combined in a fixed effects meta-analysis using the Cochrane Collaboration Review Manager software. JBI-MAStARI was not used, as per the published protocol, as it did not allow for multiple analyses to be conducted at the same time. Due to heterogeneity for one comparison/outcome, random effects meta-analysis was also used. Results of the meta-analysis are presented using odds ratio (OR) (for categorical data) and weighted mean difference (for continuous data), along with their 95% confidence intervals (CI). The presence of heterogeneity was determined using the standard Chi-square test. The degree of heterogeneity was assessed using I2. Standard deviation (SD) was calculated from the standard error of the mean (SEM) (Institute, 2008; Rosner, 2011) reported for one study (Smith, et al., 2000).

The variations between studies, particularly in relation to the variety in treatment received by control and intervention groups, and time points of temperature measurements, meant that only limited meta-analyses were possible. The remaining data were synthesized into a narrative summary. A table was developed to provide an outline of the interventions and outcomes of the included studies (see Appendix G).

Results

Description of studies

After removal of duplicates from the original searches, and title and abstract checking, 86 studies were identified. After verification of study eligibility, 24 studies were identified as potentially eligible for inclusion in the review. Following the addition of two studies identified from reference lists, 26 studies were critically appraised. Finally 12 studies remained (see Figure 1), giving a combined total of 719 participants. Full details of the excluded studies are provided together with reasons for exclusion (see Appendix H).

The 12 included studies were all RCTs. Temperature was the primary outcome in the majority of studies, but some studies of shivering were also included in which temperature was recorded as a secondary outcome.

The populations among studies were very similar - most participants underwent elective CS apart from in one study (n= 68) where 'semi-urgent' cases were also included.(Reidy, et al., 2008) Mode of anaesthesia also differed between studies but the majority included patients undergoing spinal or epidural anaesthesia rather than combined spinal-epidural (CSE) or general anaesthesia. The included studies were conducted in the United Kingdom (Chakladar, Dixon, & Harper, 2012), (Woolnough, Allam, et al., 2009), Canada (Chan, et al., 1989; Fallis, et al., 2006; Reidy, et al., 2008), Iran (Oshvandi, et al., 2011), the United States (Horn, et al., 2002),(Smith, et al., 2000), Korea (Chung, et al., 2012), India (Goyal, et al., 2011), Taiwan (Sun, et al., 2004), and Japan (Yokoyama, et al., 2009).

The method used to measure maternal core temperature varied widely between studies, with temporal artery, bladder, oral, aural infrared, tympanic thermocouple, skin and axillary measurements all utilized. Although it is acknowledged that there are issues of reliability between temperature measurement sites and core temperature, the choice of site was not used as a basis for inclusion or exclusion in this review. The findings of the review are organized according to the interventions utilized in the included studies, and within these groups, sub-headings according to outcome are used.

Once studies had been critically appraised with the appropriate JBI critical appraisal tool for experimental studies (Appendix B) and found to be of sufficient quality to include in the review by satisfying the majority of the criteria on the tool, the included studies were then further rated as high (one study) (Woolnough, Allam, et al., 2009), moderate (five studies) (Chakladar, et al., 2012; Horn, et al., 2002; Oshvandi, et al., 2011; Sun, et al., 2004; Yokoyama, et al., 2009) or low quality (six studies) (Chan, et al., 1989; Chung, et al., 2012; Fallis, et al., 2006; Goyal, et al., 2011; Reidy, et al., 2008; Smith, et al., 2000) based on the randomization methods, blinding to treatment allocation, concealment of allocation from the allocator, blinding of outcome assessors and the inclusion in the analysis of participants who withdrew from the study.

Six studies were considered to have unclear or less than rigorous randomization methods (Chung, et al., 2012; Oshvandi, et al., 2011) (Chan, et al., 1989; Reidy, et al., 2008; Smith, et al., 2000; Sun, et al., 2004). The main methods used for randomisation were computer-generated randomisation (Chakladar, et al., 2012; Goyal, et al., 2011; Horn, et al., 2002; Woolnough, Allam, et al., 2009; Yokoyama, et al., 2009) but block randomization (Fallis, et al., 2006) and card drawing (Chan, et al., 1989) were also used.

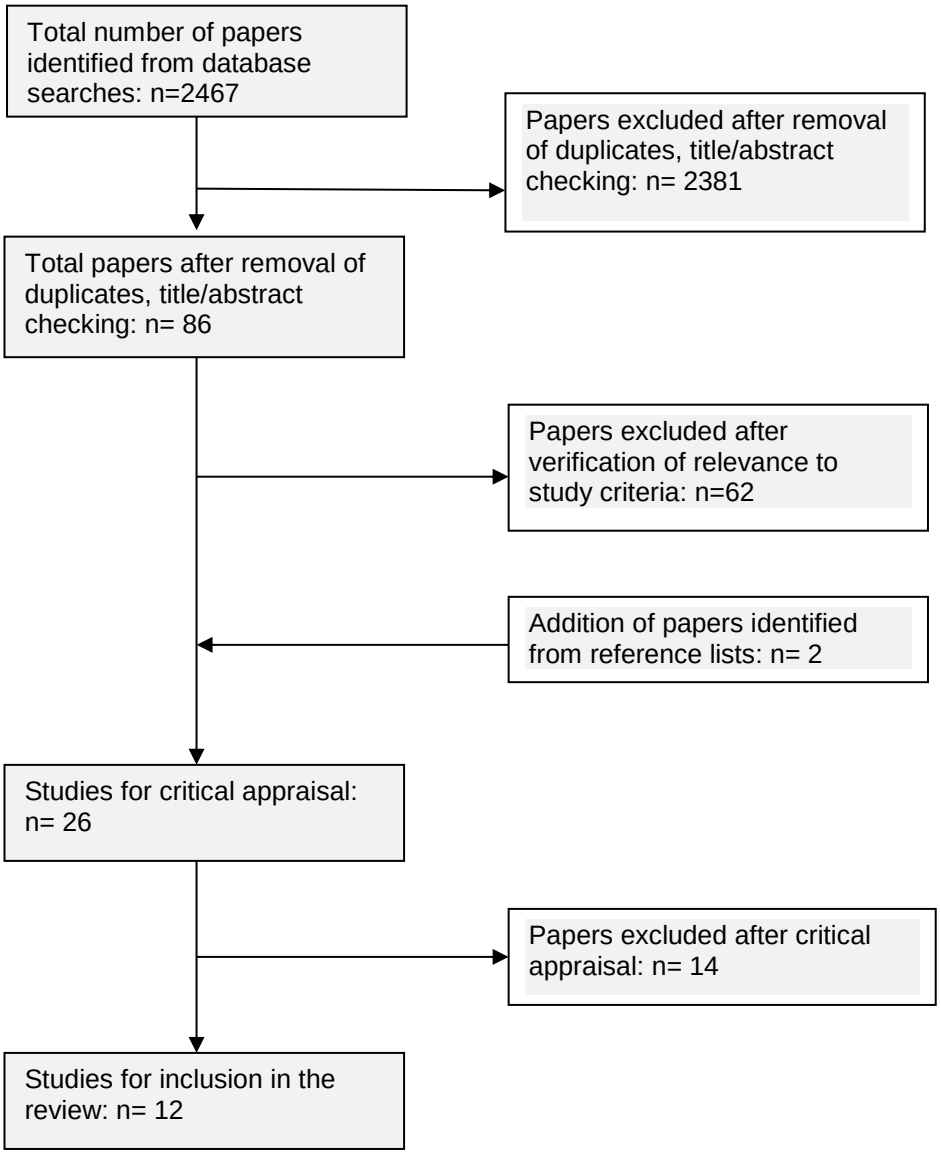

Figure 1: Flowchart of study retrieval and selection

Participant blinding was unclear or not addressed by six studies (Chan, et al., 1989; Chung, et al., 2012; Goyal, et al., 2011; Reidy, et al., 2008; Smith, et al., 2000;

Yokoyama, et al., 2009). The practical difficulties of blinding participants to the relevant interventions should be acknowledged here and depended on the nature of the intervention. Forced air warmers tend to generate noise and their use may be difficult to conceal. Lack of blinding was a common issue in the included forced air warming studies. Fallis et al. (Fallis, et al., 2006) acknowledge that the lack of participant blinding in their forced air warming study may have precipitated bias. Horn et al. (Horn, et al., 2002) also acknowledged the lack of participant blinding in their forced air warming study. Chakladar's unpublished study on the use of an under-body carbon polymer mattress was not blinded, which the authors attribute to the lack of feasibility of doing so (Chakladar, et al., 2012).

Similarly, the blinding of investigators assessing outcomes was unclear in four studies (Chan, et al., 1989; Chung, et al., 2012; Reidy, et al., 2008). In two studies it appears that while some outcomes were measured by blinded observers, it remains unclear if all the outcomes were measured by blinded observers (Smith, et al., 2000; Sun, et al., 2004). Two studies of forced air warming did not attempt to blind outcome assessors (Chakladar, et al., 2012; Fallis, et al., 2006) and this might be related to the practicalities of doing so.

Additional information was requested from five authors of included studies (Chakladar, et al., 2012; Chung, et al., 2012; Fallis, et al., 2006; Reidy, et al., 2008; Woolnough, Allam, et al., 2009) three of whom provided additional information (Chakladar, et al., 2012; Fallis, et al., 2006; Reidy, et al., 2008). This was particularly important in relation to the as yet unpublished studies (Chakladar, et al., 2012; Reidy, et al., 2008). Only limited data could be combined in meta-analysis due to the variations between studies, particularly between time points of temperature measurement. The timing of temperature measurement varied widely between studies, particularly in regard to intervals between measurements, end points (for example, some studies ceased temperature measurements at the end of surgery whilst others continued into the postoperative period) and the time point for which data was reported. Limited data reporting, and the use of figures and graphs to display results, reduced the amount of usable data that could be extracted for analysis. Where possible, specific p-values are presented but the included studies did not always report them.

Findings of the review

Intravenous fluid warming

Overview of studies

Seven included studies (Chan, et al., 1989; Chung, et al., 2012; Goyal, et al., 2011; Oshvandi, et al., 2011; Smith, et al., 2000; Woolnough, Allam, et al., 2009; Yokoyama, et al., 2009) compared intravenous fluid (IV) warming with other interventions and most of these (Chan, et al., 1989; Goyal, et al., 2011; Oshvandi, et al., 2011; Smith, et al., 2000; Yokoyama, et al., 2009) used room temperature fluids as a comparator. Two studies (Chung, et al., 2012; Woolnough, Allam, et al., 2009) used a three group design: one compared two different methods of fluid warming versus room temperature fluids (Hotline™ fluid warmer – a method which warms fluids in the IV tubing via circulating water bath during delivery to the patient – versus warming cabinet) (Woolnough, Allam, et al., 2009) and another study compared warmed IV preload versus forced air warming plus room temperature fluid preload versus room temperature fluid preload alone (Chung, et al., 2012). The use of additional interventions such as reflective ('space') blankets (Yokoyama, et al., 2009) or warmed skin preparations (Chan, et al., 1989) by two other studies to either one or both groups, limited meta-analysis. Meta-analysis was performed between comparable groups (see below) for the outcomes of mean temperature on arrival to PACU, temperature at 30 minutes in PACU and shivering.

There was a wide variation in both fluid warming methods and temperatures for administration of warmed fluids. Data extracted were not separated according to method of warming but simply as warmed or unwarmed. Warming cupboards were used to store warmed fluids in four studies (Woolnough, Allam, et al., 2009) (Chan, et al., 1989; Chung, et al., 2012; Yokoyama, et al., 2009) and the temperature settings ranged between 38-45°C. Two of these studies (Chung, et al., 2012; Woolnough, Allam, et al., 2009) measured the actual administration temperature of the fluids at the distal end when passed through the apparatus or giving set and found this to be 37-38°C. Fluid warmers were used in three studies: Hotline™ warmers in studies by Woolnough et al. (Woolnough, Allam, et al., 2009) and Smith et al. (Smith, et al., 2000) and an Astotherm™ by Goyal et al (Goyal, et al., 2011). This method warms fluids via the tubing as they pass through the device, which is situated between the IV fluid reservoir (bag) and the patient. Fluids in these studies were

warmed to 42°C (Smith, et al., 2000; Woolnough, Allam, et al., 2009) and 39°C (Goyal, et al., 2011). Water baths were also utilized as a method of fluid warming in two studies (Oshvandi, et al., 2011; Yokoyama, et al., 2009) although in one of these studies this was a secondary method of warming the IV tubing to maintain the temperature of the fluids that had been already warmed in a warming cupboard (Yokoyama, et al., 2009).

The commonly used comparator in these studies was 'room temperature' fluids and the temperature of these was unspecified in two studies (Woolnough, Allam, et al., 2009) (Chung, et al., 2012) but typically ranged in the remaining studies from 20-25°C (Chan, et al., 1989; Oshvandi, et al., 2011; Smith, et al., 2000) (Goyal, et al., 2011) (Yokoyama, et al., 2009). As stated above, the studies were not separated according to the equipment or method used to warm the fluids, but have been assessed in this systematic review according to the interventions and comparators.

Intravenous fluid warming and maintenance of maternal temperature

Maternal temperature was measured at different time points by the studies of warmed IV fluids, thus limiting comparability. The most abundant data extracted from the fluid warming studies relates to the recovery phase of care. Yokoyama et al.'s study of warmed IV fluids and reflective blanket versus unwarmed IV fluids and reflective blanket measured tympanic temperature (via thermocouple) and forearm-fingertip temperature gradient at multiple time points (Yokoyama, et al., 2009). Tympanic temperature at the time of delivery was higher in patients with warmed IV fluids compared to those with unwarmed IV fluids: 36.7°C (SD: +/- 0.3°C) versus 36.2°C (SD: +/- 0.3°C), $p < 0.05$ and remained so at 15 minutes, 30 minutes and 45 minutes after delivery: 36.4° C (SD: +/- 0.2°C) versus 35.5°C (SD +/- 0.3°C) at 45 minutes after delivery ($p<0.05$, as examined by repeated measures of analysis of variance (ANOVA). These findings also appear to be clinically significant, particularly at the 45 minute time point. In this study, it remains unclear whether the 45 minutes after delivery time point included patients who were actually in the recovery phase or were still in the operating room. Another study found that the average core temperature at the end of anaesthesia was also higher in patients administered pre-surgery warmed IV fluids versus room temperature fluids (36°C, SD: +/- 0.5°C versus 35.34°C, SD: +/- 0.06°C, $p<0.05$).

Smith et al.'s study of warmed IV fluids via Hotline versus room temperature fluids also reported multiple temperature measurement time points (using a tympanic Mon-a-Therm thermocouple) throughout the intraoperative and postoperative periods (Smith, et al., 2000). This study found a statistically significant greater number of hypothermic (<36°C) patients at the end of surgery for the unwarmed group (24/32 patients or 75%) versus 16/32 patients (46%) in the warmed group, $p < 0.05$ using Student's t test). In addition, they also found a significantly lower core final temperature for the unwarmed (control) group (35.6 °C, SD: +/- 0.7°C versus 36.1°C, SD: +/- 0.6°C in the warmed group, $p < 0.05$). Differences in the lowest temperature between groups (35.5°C, SD: +/- 0.6°C in the control group versus 36.0°C, SD: +/- 0.6°C in the warmed group, $p<0.05$) were also statistically and clinically significant.

Chan et al.'s study of warmed IV fluids plus warmed skin preparation fluids and extra clothing versus room temperature fluids found a statistically and clinically significant ($p<0.05$) lower drop in the mean aural temperature (via Mon-A-Therm™ thermocouple) and the mean bladder temperature between baseline to arrival in recovery room using student's t test (Chan, et al., 1989). Mean bladder temperature drop between baseline and arrival in recovery room was 1.0°C (SD: +/- 0.02°C) in the control group versus 0.6°C (SD: +/- 0.01°C) in the intervention group ($p<0.05$) and for aural temperature was 0.9°C (SD: +/- 0.06°C) in the control group versus 0.5°C (SD: +/- 0.04°C) in the intervention group ($p<0.05$). However the addition of these extra warming interventions in this study limits comparability with other study results.

Three studies found that administration of warmed fluid preload versus room temperature fluids (administered in the operating theatre but prior to anaesthesia) appears to result in higher temperatures when measured 60 minutes after induction of anaesthesia or in the recovery phase (Chung, et al., 2012; Oshvandi, et al., 2011; Woolnough, Allam, et al., 2009). Oshvandi et al.'s study of women undergoing elective CS under general anaesthesia found a statistically significant higher mean infrared aural temperature (using a Tympanic FT55™ thermometer) for women who received a preload of warmed intravenous fluids compared to those who received room temperature fluids (Oshvandi, et al., 2011). The mean temperature of the intervention group was 35.9°C (SD: +/- 0.5°C) compared with 35.4°C (SD: +/-

0.6°C) (p=0.001, with ANOVA) which may be less clinically than statistically significant. Similarly, the greatest temperature decrease during the 60 minutes after combined spinal-epidural (CSE) insertion in Chung et al.'s three group study (warmed fluid preload versus room temperature preload versus forced air warming) was experienced by the room temperature group (0.4°C difference, 95% confidence interval 0.2-0.6°C, p=0.015) (Chung, et al., 2012). Woolnough et al.'s three group study of warmed IV fluids via Hotline versus cabinet warmed IV fluids versus room temperature fluids reports significantly greater mean infrared aural temperature decrease (measured via ThermoScan Exac Temp thermometers) in the room temperature group during the first 60 minutes following CSE, but only results for the decrease in room temperature fluids are reported: 0.4°C (95% CI 0.2-0.6°C, p=0.015) (Woolnough, Allam, et al., 2009).

Two studies of intravenous fluid warming were combined using meta-analysis for mean temperature on arrival to PACU (Figure 2) (Goyal, et al., 2011; Smith, et al., 2000). Goyal et al. compared intravenous fluids at room temperature (22°C) with intravenous fluids warmed via a fluid warmer (to 39°C) (Goyal, et al., 2011), whilst Smith et al. also studied room temperature fluids (20-22°C) with warmed intravenous fluids (via Hotline™, 42°C) (Smith, et al., 2000). The summary estimate of these studies found that administration of warmed IV fluids compared to room temperature fluids at 20-22°C resulted in a statistically significant higher mean temperature on arrival to PACU (mean difference 0.30, 95% CI 0.11-0.49).

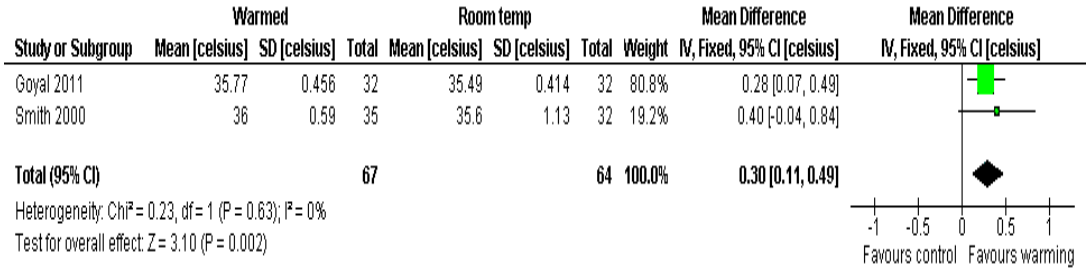

Figure 2: Intravenous fluid warming versus room temperature fluids and mean temperature on arrival to PACU

The two studies in Figure 2 (Goyal, et al., 2011; Smith, et al., 2000) were also analysed for the outcome of mean temperature after 30 minutes in PACU (Figure 3), showing the effectiveness of IV fluid warming in increasing mean temperature persisted into the recovery phase (mean difference 0.51, 95% CI 0.35-0.68).

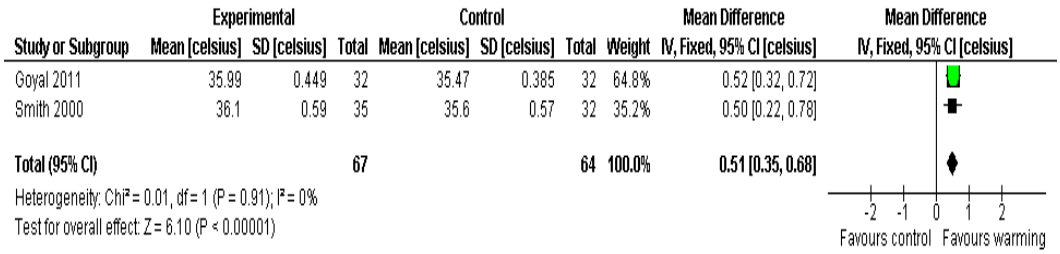

Figure 3: Intravenous fluid warming versus room temperature fluids and mean temperature at 30 minutes in PACU

Smith et al.'s study also demonstrated a statistically significantly higher maternal temperature at discharge from recovery in the warmed fluid group using Student's *t* test (36.5°C, SD: +/- 0.6°C versus 36.1°C, SD: +/- 0.6°C, $p < 0.05$), but the lack of discharge temperature time points in other studies limits comparability (Smith, et al., 2000). Both warmed IV fluids administered pre-surgery and during surgery appeared to have benefits for increasing maternal temperature, as measured in the latter intraoperative phase and into the recovery phase, until discharge.

Intravenous fluid warming and prevention of shivering

Six of the seven fluid warming studies (Chan, et al., 1989; Chung, et al., 2012; Goyal, et al., 2011; Oshvandi, et al., 2011; Smith, et al., 2000; Woolnough, Allam, et al., 2009) also measured participant shivering. In two studies dichotomous data is presented from the assessment of the presence or absence of shivering before and after CS (Goyal, et al., 2011) or in PACU (Smith, et al., 2000). In addition, details of interventions to treat the shivering once it occurred were recorded (number and type) (Goyal, et al., 2011; Smith, et al., 2000). Similar four-point scales recording the degree of shivering intensity were used by two studies, (Woolnough, Allam, et al., 2009) (Chan, et al., 1989) while a five point scale was used by Oshvandi et al. (Oshvandi, et al., 2011) (attributed to Crossley and Mahajan) (Crossley & Mahajan, 1994) and a four point scale was used by Chung et al (Chung, et al., 2012) (attributed to Wrench) (Wrench, et al., 1997). Three studies utilizing shivering scales also reported on presence and absence of shivering (Chung, et al., 2012; Oshvandi, et al., 2011; Woolnough, Allam, et al., 2009).

The single study that compared an intervention of warmed fluids, warmed skin preparation and additional clothing with another intervention of room temperature fluids, room temperature skin preparation and single hospital gown (Chan, et al., 1989) could not be included in the meta-analysis (because of the extra interventions) and did not find a significant difference in incidence of shivering between groups (11 of 21 patients reported shivering in the intervention group versus 13/19 in control group, no p value reported). Five studies comparing IV fluid warming with room temperature fluids were combined in a meta-analysis of effectiveness warmed IV fluids on the incidence of shivering (Chung, et al., 2012; Goyal, et al., 2011; Oshvandi, et al., 2011; Smith, et al., 2000; Woolnough, Allam, et al., 2009) (Figure 4).

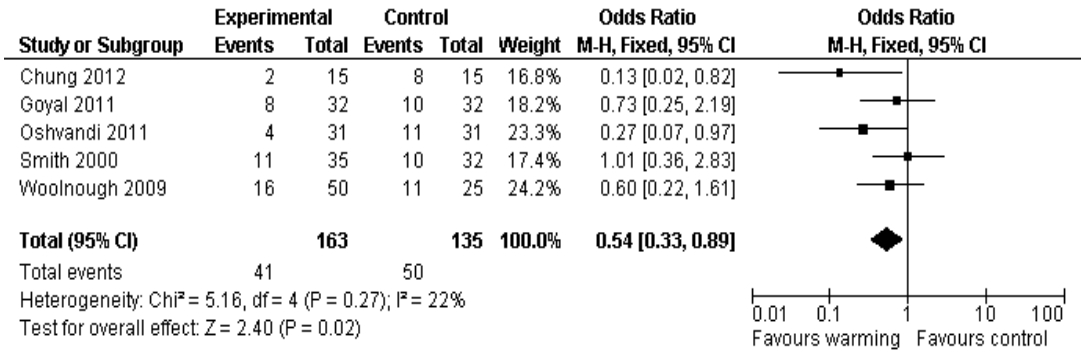

Figure 4: Intravenous fluid warming versus room temperature fluids and the incidence of shivering

Two of the three groups in Oshvandi et al.'s study, the warmed IV fluid and room temperature groups (Oshvandi, et al., 2011), were included in this meta-analysis, as per advice for managing multiple-group studies in the Cochrane Handbook for Systematic Reviews of Interventions (Deeks, et al., 2011). In addition, for Woolnough et al.'s three group study the two warmed fluid groups were combined together, as the interventions were sufficiently similar, and compared to the room temperature group (Woolnough, Allam, et al., 2009). The combined result significantly favours intravenous fluid warming (OR 0.54, 95% CI 0.33-0.89) for reducing shivering in this population.

Intravenous fluid warming and maternal thermal comfort

Maternal thermal comfort was assessed by both of the three group studies (Chung, et al., 2012; Woolnough, Allam, et al., 2009). Woolnough et al.'s study of Hotline™ warmed fluids versus warming cabinet fluids versus room temperature fluids used a 0-10 numerical rating scale with 0 indicating 'worst imaginable cold', 5 as 'thermally neutral/comfortable' and 10 indicating 'insufferably hot' (Woolnough, Allam, et al., 2009). The authors considered a score of less than 4 to correspond to feeling cold, whilst a score of more than 6 corresponded to feeling hot. Similarly, Chung et al.'s three group study of warmed IV preload versus unwarmed IV preload (and versus upper body forced air prewarming) which used a 100mm Visual Analogue Scale (VAS) with 0mm indicating 'insufferably hot', 50mm 'thermally neutral' and 100mm as 'worst imaginable cold', reported on thermal discomfort (reporting on data for cold VAS scores between 50mm-100mm) (Chung, et al., 2012).

There was a statistically significant difference in the number of patients reporting thermal discomfort (a thermal comfort score of <4) between the three groups in Woolnough et al.'s three group study (p=0.32) although the statistical test is not specified (Woolnough, Allam, et al., 2009). In the room temperature fluids group: 8/25 (32%) scored <4, whereas 3/25 (12%) scored <4 in the warming cabinet group and only 1/25 (4%) scored <4 in the Hotline group (Woolnough, Allam, et al., 2009). This also appears to be clinically significant: in this study patients appear to demonstrate greater thermal comfort if receiving warmed intravenous fluids. No statistically significant difference or clinically significant (p= 0.093) difference in maternal thermal comfort was found between preload of warmed IV fluid, upper body forced air warming with room temperature preload and room temperature preload (no warming) in Chung et al.'s study with cold VAS data reported (59.3mm, SD: 13.2mm versus 59.0mm, SD: 12.1mm versus 69.0mm, SD: 15.9mm respectively) (Chung, et al., 2012). There were differences between these studies in relation to the temperature settings of fluid warming devices: fluids in Chung et al.'s study were warmed to 40°C via a warming cabinet (Chung, et al., 2012), whereas in Woolnough et al.'s study which found a significant difference in thermal comfort from warmed fluids, warming cabinet fluids were stored at 45°C and Hotline™ fluids were set to 42°C (Woolnough, Allam, et al., 2009). Greater volumes of fluid were infused in Woolnough et al.'s study (2.0 litres, SD: 0.4 litres in the room

temperature group, 2.1 litres, SD: 0.4 litres in the warming cabinet group and 2.4 litres, SD: 1.4 litres in the Hotline group) (Woolnough, Allam, et al., 2009) as opposed to Chung et al.'s study (1.1litres, SD: 0.1litres in the room temperature group, 1.2 litres, SD: 0.2litres in the warmed fluid preload group and 1.2litres, SD: 0.1 litres in the forced air warming group) (Chung, et al., 2012).

These differing results could also be examined in the context of what 'room temperature' refers to in each study. Chung et al.'s study did not report data on ambient temperature (Chung, et al., 2012), whereas Woolnough et al. report that ambient temperature was 24.2°C (SD: +/- 0.9°C) in the room temperature group, 23.9°C (SD: +/-1.4°C) in the warming cabinet group and 24.2 °C (SD: +/-0.8°C) in the Hotline group (Woolnough, Allam, et al., 2009). Woolnough et al. did not examine the differences in ambient temperature between groups in this study (Woolnough, Allam, et al., 2009). Thus it remains unclear whether differences in ambient temperature play a role in the conflicting results between these studies.

Intravenous warmed fluids and time to discharge from PACU

Time to discharge from PACU was assessed only in two IV fluid warming studies (Goyal, et al., 2011; Smith, et al., 2000) but for one (Smith, et al., 2000) it remains unclear whether time to discharge as reported actually refers to time to fitness for discharge, or actual time to discharge (which may be dependent on many external factors, such as availability of ward staff).

Goyal et al.'s study of warmed IV fluids versus room temperature IV fluids found no statistically significant difference in PACU discharge times in minutes (min) between groups: 105.5min (SD: +/- 9.5min) in the room temperature group versus 107.3min (SD: +/- 9.2min) in the intervention group (Goyal, et al., 2011). Similarly, Smith et al.'s study of warmed IV fluids versus room temperature IV fluids found no significant difference in time to PACU discharge in minutes between groups: 109min (SD: 6min) in the intervention group versus 103min (SD: +/- 7min) in the control group (no p value was reported) (Smith, et al., 2000). The administration of intraoperative warmed IV fluids does not appear to shorten PACU stays for patients.

Intravenous fluid warming and neonatal outcomes

Apgar scores.

Apgar scores were evaluated by a paediatrician at one minute after delivery in two IV warming studies, both also using reflective blankets (Chung, et al., 2012; Yokoyama, et al., 2009) but these two studies could not be combined in meta-analysis due to clinical heterogeneity. While study groups were similar in both studies, there were differences between studies in the temperature of warmed fluids, methods of administering warmed fluids and methods of temperature measurement. The Apgar score was significantly higher for the warmed IV fluids group in Yokoyama et al.'s study in comparison to the room temperature fluids group (Yokoyama, et al., 2009). Whereas in Chung et al.'s three group study the Apgar score was lower, but not significantly, for the warmed IV fluid preload compared to the room temperature fluid preload and the upper body forced air warming groups (see Table 1) (Chung, et al., 2012).

Table 1: Apgar scores at one minute – IV fluid warming

Study	Apgar score at one minute			
	Warmed IV fluid*	Room temperature fluids*	Upper body forced air warming	p value
Yokoyama et al. (2009) ^	9 (8-9)	8 (8-9)	n/a	0.029 (Mann-Whitney U-test)
Chung et al. (2012) # *preload	8.07 ± 1.10	8.20 ± 0.86	8.13 ± 0.86	0.927* (statistical test not specified)

^ median (range), # mean (SD)* across three groups

No significant difference in Apgar score between groups at five minutes after delivery (p= 0.18) was found by Yokoyama et al. (Table 2), in contrast to the statistically significant result for Apgar scores at one minute (Yokoyama, et al., 2009).

Table 2: Apgar scores at five minutes – IV fluid warming versus room temperature fluids (Yokoyama et al., 2009)

Study - Yokoyama et al. (2009)	Apgar Score at five minutes (number/total number)		
Apgar score	Warmed IV fluids	Room temperature fluids	p value Mann-Whitney U-test
8	1/15	0/15	0.18
9	12/15	15/15	
10	2/15	0/15	

Umbilical pH

While umbilical pH was also evaluated in the same two IV fluid warming studies that compared Apgar scores, these could not be combined due to clinical heterogeneity because of the source of blood for pH measurement. Chung et al. measured umbilical vein pH immediately after birth (Chung, et al., 2012), whilst Yokoyama et al. measured umbilical artery pH (Yokoyama, et al., 2009). Yokoyama et al. reported a statistically significantly higher pH for the warmed IV fluid group in comparison to the room temperature fluid group but there is little clinical significance to these results (Yokoyama, et al., 2009), while Chung et al.'s study found no statistically or clinically significant difference between the three groups receiving warming (Chung, et al., 2012) (Table 3). Yokoyama et al. also reported that umbilical pH data were averaged according to the number of patients receiving ephedrine (five participants in both groups) (Yokoyama, et al., 2009), but it is unclear as to what this refers to.

Table 3: Umbilical pH – IV fluid warming versus room temperature fluids

Study	Umbilical pH: artery (Yokoyama et al. 2009)/ vein (Chung et al. 2012)			p value
	Warmed IV fluids*^	Room temperature fluids*^	Upper body forced air warming^	
Yokoyama et al (2009)	7.33 ± 0.045	7.29 ± 0.034	n/a	0.023 (via analysis of covariance)
Chung et al (2012) *preload	7.33 ± 0.06	7.35 ± 0.04	7.32 ± 0.04	0.349 (statistical test not specified)

^ mean ± SD

Neonatal temperature

Of the fluid warming studies, the only study that measured newborn temperature via the rectal route at five minutes after delivery (and after newborn head wrapping and placement under radiant heater) found no statistically or clinically significant difference (p=0.16 Student's t test) between groups (37.2°C, SD: +/- 0.3°C in the warmed fluid group versus 37.0°C, SD: +/- 0.4°C in the unwarmed fluid group) (Yokoyama, et al., 2009). Again, neonatal temperature data in Yokoyama et al.'s study was averaged according to the number of patients receiving ephedrine (Yokoyama, et al., 2009).

Summary

Warmed IV fluids are effective at improving maternal temperature whether administered pre or intraoperatively, and are also effective at reducing shivering. It remains unclear whether warmed IV fluids have a positive effect on maternal thermal comfort, umbilical pH or Apgar scores. This intervention was also not found to improve newborn temperature at birth or reduce time to discharge from PACU.

Warming devices: covers and mattresses

Overview of studies

Five studies compared warming devices with other interventions (Table 4). Chung et al. used a three group design with upper body forced air prewarming plus unwarmed IV fluid preload versus warmed IV fluid preload with no forced air warming versus unwarmed fluid preload with no forced air warming (Chung, et al., 2012). The remaining four studies used a two group design (Chakladar, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002; Reidy, et al., 2008).

Three studies utilized upper body forced air warming (Horn, et al., 2002) (Chung, et al., 2012; Fallis, et al., 2006) via Bair Hugger™ devices. Clinical heterogeneity that limited comparability between these studies included: outcomes measured at different time points and also likely key differences between interventions and comparators. Fallis et al. utilized intraoperative forced air warming post insertion of spinal anaesthesia, once patients were supine (Fallis, et al., 2006), whereas Chung et al. utilized 15 minutes of preoperative forced air warming (Chung, et al., 2012) and

Horn et al. utilized both a 15-minute preoperative warming period and continued with intraoperative forced air warming (Horn, et al., 2002). *Warmed c*otton blankets were used as a comparator by Fallis et al. (Fallis, et al., 2006) whereas *unwarmed* cotton blankets were used by Horn (Horn, et al., 2002). As described earlier, Chung et al.'s study utilized a three group design with warmed or unwarmed IV fluids comparison groups, with both of these groups receiving identical forced air warming blankets with the unit switched off (Chung, et al., 2012).

Table 4: Forced air warming studies – intervention and comparison groups

Study	Intervention/s		Control		Control 2	
	Forced air warming	Warmed IV fluids	Covering/ blanket	Warmed IV fluids	Covering/ blanket	Warmed IV fluids
Fallis et al. 2006	Upper body forced air warming	Yes	Warmed cotton blanket	Yes	n/a	n/a
Horn et al 2002	Upper body forced air warming	Yes	Single cotton blanket	Yes	n/a	n/a
Chung et al. 2012	Upper body forced air warming	No	Forced air warming blanket switched OFF	Yes	Forced air warming blanket switched OFF	No
Chakladar et al. 2012	Under-body carbon polymer warming switched ON	Yes	Carbon polymer warming blanket switched OFF	Yes	n/a	n/a
Reidy et al. 2008	Under-body forced air warming	Yes	'standard care' warmed cotton blankets	Yes	n/a	n/a

All of the above studies used a 43°C setting for the warming devices. In Fallis et al.'s study (Fallis, et al., 2006) however, one participant commenced at 38°C before progressing to the high setting and 14 of 32 participants also subsequently adjusted to a lower setting.

Two unpublished studies (Chakladar, et al., 2012; Reidy, et al., 2008) investigated the effectiveness of full under-body warming mattresses (Table 4), utilizing forced air warming (Reidy, et al., 2008) and carbon polymer (Chakladar, et al., 2012) mattresses. Data available in these as yet unpublished studies was minimal and therefore additional data was requested from both authors. Additional information obtained from the authors revealed that the mattress temperature settings in these studies also differed, with settings of 38°C (Reidy, et al., 2008) and 40°C (Chakladar, et al., 2012). As described, clinical heterogeneity contributed to the inappropriateness of meta-analysis for the warming device studies. Data is therefore largely presented by means of narrative analysis.

Warming devices and maintenance of maternal temperature

Data enabling the assessment of the effectiveness of forced air and carbon polymer mattress warming on maintaining maternal temperature were not abundant. As stated above, data were especially lacking from the as yet unpublished studies (Chakladar, et al., 2012; Reidy, et al., 2008) and additional data were obtained from the studies' authors.

Chakladar et al.'s study of a carbon polymer mattress turned on (40°C) versus carbon polymer warming mattress turned off (and warmed IV fluids to 41°C in both groups) presented useful data relating to the incidence of IPH (temperature <36°C) in both groups (Chakladar, et al., 2012). The authors found a significantly lower incidence of IPH in the intervention group (3/58 participants) versus the control group (11/58 participants, $p = 0.043$, but the statistical test was not specified).

Reidy et al.'s study of a forced air warming mattress versus 'standard care' (as described above) also found a significant difference between groups in relation to mean maternal temperature on entering PACU: 36.1°C (SD +/- 0.4°C) in the intervention group versus 35.7°C (SD +/- 0.5°C) in the control group ($p=0.01$). No other maternal temperature data was available from this study (Reidy, et al., 2008). Although it is unfortunate that only minimal maternal temperature data is available from this study, the summary estimate of the two studies when combined using random effects meta-analysis favour under-body warming, in comparison to warmed cotton blankets or warmed IV fluids alone, for initial admission temperature to PACU (Figure 5) (mean difference 0.29, 95% CI 0.09 to 0.48).

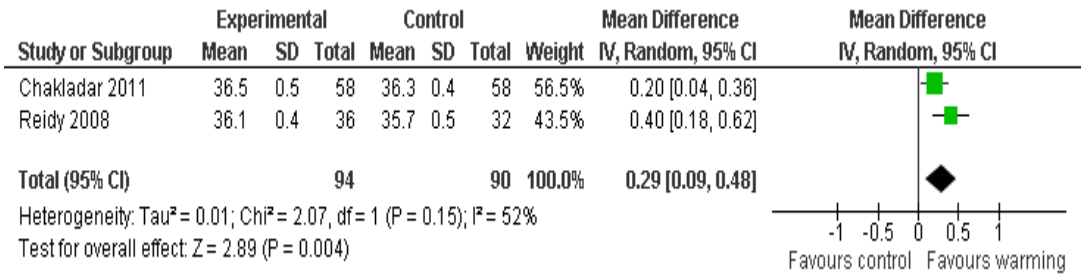

Figure 5: Under-body warming mattress versus control and temperature (°C) on arrival to PACU.

The I^2 value (Figure 5) above suggests moderate heterogeneity (Deeks, et al., 2011) In consideration of possible explanations, it should be noted that there are some differences in the interventions. While both studies utilized under-body warming, the devices differed (a carbon polymer mattress in Chakladar et al.'s study (Chakladar, et al., 2012), and a forced air mattress in Reidy et al.'s study (Reidy, et al., 2008). In addition, Chakladar et al. used a setting of 40°C (Chakladar, et al., 2012) while the other study used a setting of 38°C, as mentioned earlier (Reidy, et al., 2008). Treatment of the control groups also varied slightly: control participants in Chakladar's study received the under-body mattress turned off and warmed IV fluids (Chakladar, et al., 2012), whereas in Reidy et al.'s study the control group received two warmed cotton blankets (initially, with the potential for more) plus warmed IV fluids (Reidy, et al., 2008). Mode of temperature measurement also differed, with temporal artery measurements used by Chakladar et al. (Chakladar, et al., 2012) and oral measurements used by Reidy et al (Reidy, et al., 2008).

Although Chung et al.'s three group study does report significant differences between the group's skin (arm) temperatures at 15 and 30 minutes after prewarming (Chung, et al., 2012), peripheral temperature is not an outcome considered by this review (although it may be closely related to thermal comfort). This study does, however, report on statistically significant differences between 'core' temperature decreases (as measured by aural infrared thermometry) at 45 minutes, reporting that there was less temperature decrease in the warmed IV fluid and forced air warming groups than the control group: a temperature decrease of -0.6°C (SD: +/- 0.4°C) in the forced air warming group versus a temperature decrease of -0.5°C (SD: +/- 0.3°C) in the warmed IV fluid group versus -0.9°C (SD: +/- 0.4°C) in the control

(room temperature and no forced air warming) group (p=0.004, but the statistical test is not specified).

Fallis et al.'s study of intraoperative upper body forced air warming also reported mean oral temperature decrease during the procedure but data after 60 minutes was omitted due to decreased sample size (Fallis, et al., 2006). Mean temperature decrease between the measured time periods was not statistically or clinically significant between the groups: -0.8°C (SD: +/- 0.5°C) for the control group versus -0.7°C (SD: +/-0.4°C) for the intervention group (p=0.508, via repeated measures ANOVA). Similarly, difference in the mean final temperature on exit from the operating theatre was not statistically significant between the groups: 35.9°C (SD: +/- 0.4°C) in the control group versus 36.1°C (SD: +/- 0.4°C) in the intervention group (p=0.189).

Horn et al.'s study of prewarming (Horn, et al., 2002) also presents data on final operating theatre temperature (as measured via Mon-a-Therm™ tympanic thermocouple) but found that patients in the forced air warming group had statistically significantly higher temperatures: 36.1°C (SD +/- 0.5°C) in the control group versus 37.1°C (SD: +/- 0.4°C) in the intervention group (p<0.001).

These results suggest that forced air preoperative warming plus intraoperative warming is more effective at intraoperative forced air warming alone in relation to maintaining maternal intraoperative temperature but there are other differences between the studies which should be considered (Table 5), such as ambient operating theatre between the studies and mode of anaesthesia (in addition to opioid administration).

Table 5: Upper body forced air warming, final maternal OT temperature and variations between studies

Study	Ambient OT temp* (°C)		Anaesthetic Mode	Opioid	Warming (timing)	Final maternal temperature in OT * (°C)		
	Interventi-on	Control				Interve-ntion	Control	*P* value
Fallis et al., 2006	Entrance: 21.6 ± 1.2. Exit: 23 ± 1.2.	Entrance: 21.6 ± 0.9 Exit: 22.2 ±0.6	Spinal	Intrathecal morphine Fentanyl citrate	Intraopera-tive	36.1°C± 0.4°C	35.9°C ± 0.4°C	NS (via independent t test)
Horn et al., 2002	23.9± 0.5	24.1 ± 0.3	Epidural	Nil	Preoperati-ve and intraopera-tive	37.1°C ± SD 0.4°C	36.0°C ± 0.5°C	<0.05 (via Student's *t* test)

* * mean ± SD

Clear differences in the characteristics of the studies are evident. Ambient operating theatre temperature appears to be warmer in Horn et al.'s study (Horn, et al., 2002) (Table 4), but mode of anaesthesia and opioid administration also differs between the studies. Duration of surgery or intraoperative time was not entered into this table due to variations in the reporting of this between the two studies (Fallis et al. report time spent in the operating theatre, whereas Horn et al. report duration of surgery, although this is another contrasting factor between the studies) (Fallis, et al., 2006; Horn, et al., 2002). Participants in Horn et al.'s study received only passive insulation in the form of cotton blankets (Horn, et al., 2002), whereas the blankets applied in Fallis et al.'s study were warmed (Fallis, et al., 2006). Forced air warming was commenced preoperatively in Horn's study (Horn, et al., 2002) but warming in the latter study was applied intraoperatively only. In addition, method of temperature measurement also differed. Tympanic thermocouples were used by Horn (Horn, et al., 2002) and oral electronic thermometers were used by Fallis et al (Fallis, et al., 2006).

Forced air warming largely appears to provide positive results in maintaining maternal temperature during CS, but the strongest results thus far appear to be achieved from applying warming in the preoperative phase of care. Under-body warming mattresses have also achieved higher maternal core temperatures when compared with warmed cotton blankets or warming mattress switched off, although there are few studies available examining under-body warming.

Warming devices and prevention of shivering

Three of the five forced air warming studies included shivering as a secondary outcome (Horn, et al., 2002) (Chung, et al., 2012; Fallis, et al., 2006) Dichotomous data is presented in terms of presence or absence of shivering, but two studies (Horn, et al., 2002) (Fallis, et al., 2006) also present ordinal data in relation to intensity of shivering (slight, moderate/intensive shivering). These two studies (Horn, et al., 2002) (Fallis, et al., 2006) use the same four-point shivering scale (0=no shivering, 1=mild shivering, 2=moderate shivering, 3=severe shivering) as used by Chan et al.'s study of warmed IV fluids effect on temperature and shivering in women undergoing CS (Chan, et al., 1989). Details of these two studies are presented in Table 6. Chung et al.'s three-group study (Chung, et al., 2012) uses an alternative four-point scale with different descriptors (referenced to Wrench 1997) (Wrench, et al., 1997) and was not entered into the table due to its three-group design and the different scale used for assessing shivering. Again, clinical heterogeneity prevented meta-analysis of these studies in relation to shivering.

Possible bias resulting from unblinded investigators assessing shivering in two of the studies (Horn, et al., 2002) (Fallis, et al., 2006) should be highlighted. Blinding of investigators is unclear in the remaining study (Chung, et al., 2012). Shivering assessment took place both during and after surgery (Chung, et al., 2012) and after every 15-minute temperature measurement (Horn, et al., 2002) (Fallis, et al., 2006).

Fallis et al. (Fallis, et al., 2006) and Horn (Horn, et al., 2002) again present differing results in relation to the effectiveness of upper body forced air warming but this time related to the presence of shivering: Fallis et al. report that there was no statistically significant difference between groups (Fallis, et al., 2006) whereas Horn et al. found that there was a significantly lower level of shivering presence in the preoperative forced air warming group (Horn, et al., 2002) (Table 6). These results can also be considered in light of the other characteristics of these studies presented in Table 5 and discussed above.

Table 6: Presence of shivering in preoperative upper body forced air warming studies

Study	Presence of shivering		p value
	Upper body forced air warming	Control	
Fallis et al. (2006)	10/32	10/30	p=0.861 (Mantel-Haenszel test)
Horn et al. (2002)	2/15	9/15	p<0.05 (Fisher's exact test)

Results from Chung et al.'s three group study also support the effectiveness of preoperative forced air warming in reducing shivering to 20% (3/15) but not to the extent of warmed IV fluids in which 13% (2/15) experienced shivering versus 53.3% (8/15) in the room temperature fluid group (p=0.035) (Chung, et al., 2012).

Results from these studies (Horn, et al., 2002) (Chung, et al., 2012; Fallis, et al., 2006) suggest that forced air warming applied in the preoperative phase of care reduces shivering, but forced air warming applied intraoperatively may have less effect on reducing shivering.

Warming devices and thermal comfort

Maternal thermal comfort was measured by the four (Horn, et al., 2002; Reidy, et al., 2008) (Chung, et al., 2012; Fallis, et al., 2006) forced air warming studies, with continuous data gained from the utilization of self-reported thermal comfort scales. Descriptors of thermal comfort status were common between three studies: 'worst imaginable cold', 'thermally neutral' and 'insufferably hot'; but again narrative summary only is possible due to clinical heterogeneity in relation to slight variations in interventions and controls between the studies (Chung, et al., 2012; Fallis, et al., 2006; Horn, et al., 2002).

Chung et al. and Horn et al. (Horn, et al., 2002) both used a 100mm Visual Analogue Scale (VAS) but with hot/cold scores reversed between the studies (for example, 0 = cold on Horn's scale but 0 = hot on Chung's scale) (Chung, et al., 2012; Horn, et al., 2002). Fallis et al. used a 0-10 scale with the above descriptors, with 0 referring to cold and 10 referring to hot (Fallis, et al., 2006). Thermal comfort scores were assessed at 15-minute intervals throughout surgery in both Horn and Fallis et al.'s studies (Fallis, et al., 2006; Horn, et al., 2002)but time points of thermal comfort assessment remain unclear in the remaining two studies (Chung, et al., 2012; Reidy,

et al., 2008). Additional information was obtained from Fallis et al. in relation to their thermal comfort data, as no data could be extracted from the figures presented in the original published article (Fallis, et al., 2006).

Reidy et al.'s study of an under-body forced air warming mattress versus 'standard care' used a three point Likert scale (with responses of 'too cold', 'comfortable', 'too hot') and reports that maternal thermal comfort did not increase (Reidy, et al., 2008), although no data is provided for this outcome. Again, the risk of bias arising from the lack of blinding of investigators assessing thermal comfort needs to be recognized, but with consideration of the practical difficulties of blinding both patients and investigators to forced air warming. The other under-body warming mattress study in this review did not measure thermal comfort but it is interesting to note that further data obtained from the authors confirms that the intervention was discontinued for one patient in the warming group due to the patient feeling hot.

VAS scores were not statistically or clinically significantly different between groups in Chung et al.'s three group study comparing preoperative upper body forced air warming, warmed IV fluid preload and room temperature fluids: 59.0mm (SD: 12.1mm) in the forced air warming group versus 59.3mm (SD 13.2mm) in the warmed IV fluid preload versus 69.0mm (SD: 15.9mm) in the room temperature fluid group (p=0.927, but statistical test not specified) (Chung, et al., 2012), although the latter group's thermal comfort appeared to be warmer.

Horn et al. reports data for thermal comfort after 15 minutes of treatment: 52mm (SD: 9mm) in the control group versus 63mm (SD: 11mm) but reports that there were no statistically significant differences in thermal comfort between the groups at other time points (Horn, et al., 2002).

Contrastingly, Fallis et al.'s study of intraoperative forced air warming found statistically and clinically significant differences in thermal comfort between the study groups in favour of intraoperative warming at 30, 45, 60 and 75 minutes (although at the 75 minute time interval, subject numbers were greatly reduced in both groups) (Fallis, et al., 2006). No data is provided for the 15 minute interval which would facilitate comparison with Horn et al.'s study (Horn, et al., 2002) and vice versa no data for further time intervals were provided by Horn et al (Horn, et al., 2002). Thermal comfort scores were consistently lower in the control group in Fallis et al.'s study (Fallis, et al., 2006) (Table 7).

Table 7: Thermal comfort scores: intraoperative upper body forced air warming (Fallis et al 2006)

Time (mins)	Sample size	Thermal comfort scores (0=cold to 10 =hot)		P value (repeated measures ANOVA)
		Intervention: upper body forced air warming	Control: warmed cotton blanket	
		Mean ± SD	Mean ± SD	
30	62	5.7 ± 0.3	4.8 ± 0.3	0.016
45	52	6.3 ± 0.3	4.84 ± 0.3	<0.001
60	37	5.8± 0.4	4.6 ± 0.3	0.014
75	17	5.5 ± 0.3	4.5 ± 0.3	0.045

Again, the characteristics of both Horn et al.'s and Fallis et al.'s studies (Table 4) are interesting in the context of these varying results, especially in relation to ambient temperature (Fallis, et al., 2006; Horn, et al., 2002). Ambient temperature on entrance to the operating theatre was lower in Fallis et al.'s study (Fallis, et al., 2006) – a cooler environment may mean that greater thermal comfort could be gained from the application of a warming device. It is also worth noting that 14 women in Fallis et al.'s study requested that the warming device be lowered to a reduced temperature setting during surgery (Fallis, et al., 2006) suggesting that thermal comfort, in terms of feeling too hot, was not optimal for these women throughout surgery.

Results on the effectiveness of forced air warming on maternal comfort are, therefore, inconclusive with varying results between studies. The relationship between ambient temperature and the possibly linked receptiveness of patients to forced air warming should be considered, as should the possibility of high forced air warming settings being intolerable for some patients.

Warming devices and time to discharge from PACU

Time to discharge from PACU was not an outcome of interest in the included warming mattress and coverings studies.

Warming devices and neonatal outcomes

Apgar scores

Apgar scores measured at one minute were an outcome of interest in four studies (Horn, et al., 2002) (Reidy, et al., 2008) (Chung, et al., 2012; Fallis, et al., 2006). Two studies measured Apgar scores at five minutes (Horn, et al., 2002) (Chung, et al., 2012) and one continued to report at ten minutes (Horn, et al., 2002). A paediatrician determined Apgar scores in both Chung et al.'s and Horn et al.'s studies (Chung, et al., 2012; Horn, et al., 2002) but it is unclear which healthcare professional measured Apgar scores in the remaining two studies (Reidy, et al., 2008) (Fallis, et al., 2006). No significant difference in Apgar scores between groups in any of the above studies was found.

Reidy's study of maternal under-body forced air warming mattress (Reidy, et al., 2008) found no statistically significant effect on Apgar scores at one or five minutes: the median Apgar score at one minute was 9 (range 6-10) in the intervention group versus 9 (range 4-10) for the control group (p=0.12, the statistical test was not specified), and median Apgar score at five minutes was 9 (range 8-10) in the intervention group, and 9 (range 9-10) in the control group (p=0.12, the statistical test was not specified).

Upper body forced air prewarming versus warmed IV fluid preload versus room temperature preload and no forced air warming (Chung, et al., 2012) also found no statistical or clinically significant difference in mean Apgar scores at one minute between groups (8.1, SD: +/- 0.8 in the upper body warming group versus 8.1, SD: +/-1.1 in the warmed IV fluid group versus 8.2, SD: +/-0.9 in the room temperature group, p=0.927 via analysis of variance). Intraoperative forced air warming also demonstrated no statistically or clinically significant difference in Apgar scores at one and five minutes (Fallis, et al., 2006): median 8 (range 5-9) for the intervention group, median 8.5 (range 3-9) for the control group at one minute and median 9 (range 8-9) for the intervention group, 9 (8-9) for the control group at five minutes (although no p value is provided and it is not clear what statistical test was used).

Again, results were similar between groups, and no statistically or clinically significant difference was found in the upper body forced air prewarming study (Horn, et al., 2002) that measured Apgar at one, five and ten minutes: at one minute,

9/15 patients obtained an Apgar of 9 in the warmed group, and 9/15 obtained an Apgar of 9 in the control group (no p values reported). It therefore appears that forced air warming does not appear to either increase or decrease Apgar scores at one or five minutes.

Umbilical pH

Umbilical pH was also assessed by the four studies above (in which Apgar score was also assessed). Both Chung et al. and Horn et al. both measured umbilical vein pH directly after birth (Chung, et al., 2012; Horn, et al., 2002). Fallis et al. and Reidy et al. also measured umbilical vein pH (Fallis, et al., 2006; Reidy, et al., 2008) but the time at which this occurred was not reported. Again, these studies could not be combined for meta-analysis due to key differences in interventions and controls, thus a narrative analysis is presented. Chung et al.'s three group study (with a sample size of 15 participants in each of the three groups) found no significant difference in umbilical vein pH measured directly after birth between the three groups (7.3, SD: +/- 0.04 in the forced air warming group versus 7.3, SD: +/- 0.06 in the warmed IV fluid group versus 7.4, SD: +/-0.04 in the room temperature fluid group, p= 0.35 via analysis of variance) (Chung, et al., 2012).

The remaining three studies are presented in Table 8. As with Chung et al.'s study (Chung, et al., 2012) both studies by Fallis (Fallis, et al., 2006) and Reidy (Reidy, et al., 2008) found no benefit from maternal forced air warming in regards to umbilical pH. Horn et al.'s study of upper body prewarming presents contrasting results and found that umbilical vein pH was significantly improved in babies born to mothers in the warmed group (Horn, et al., 2002) (see Table 6), with babies in the control groups having a mean umbilical vein pH of 7.24 (SD ± 0.07) versus a mean umbilical vein pH of 7.32 (SD ±0.07) in the intervention group. Information regarding gestation in weeks is not provided by Horn et al. (Horn, et al., 2002) but participants were 'healthy' and booked for elective surgery, suggesting that gestation or maternal medical history may not be relevant in the respect of differences in neonatal outcomes in this study. Both Horn et al. (Horn, et al., 2002) and Chung et al. (Chung, et al., 2012) utilized preoperative warming but with differing results. It remains unclear whether forced air warming, in particular when applied during the preoperative phase of care, improves umbilical pH.

Table 8: Umbilical vein pH and forced air warming

Study	Umbilical vein pH #			P value
	Upper body forced air warming*	Under-body forced air warming mattress	Control	
	Mean ± SD	Mean ± SD	Mean ± SD	
Fallis et al. (2006)	7.30 ± 0.0^ (n= 31)	n/a	7.30 ± 0.0^ (n= 28)	Not provided
Horn et al. (2002)*	7.32 ± 0.07 (n=15)	n/a	7.24 ± 0.07 (n=15)	<0.05 (one-way analysis of variance)
Reidy et al. (2008)	n/a	7.30 ± 0.1 (n=36)	7.30 ± 0.04 (n=32)	0.09 (statistical test not specified)

Mean ± SD; ^ SD 0.0 taken directly from article; *applied preoperatively

Neonatal temperature

Three of the forced air warming studies also measured neonatal temperature, either as rectal temperature at delivery (Horn, et al., 2002) (Fallis, et al., 2006) or axillary temperature one minute after delivery(Reidy, et al., 2008). In Reidy et al.'s study of the use of forced air warming mattress neonatal temperature was a primary outcome but the study found no statistically or clinically significant difference in neonatal temperature between the warmed and control groups (Reidy, et al., 2008). Mean neonatal axillary temperature at one minute was 36.8°C (SD: +/- 0.3°C) in the warmed group versus 36.9 °C (SD: +/- 0.3°C) in the control group (p= 0.40). The authors report that temperature was also checked at five and ten minutes after delivery but no data was available for inclusion in this review.

Mean newborn rectal temperature was found to be 37.7°C (SD: +/- 0.4°C) in the warmed group (of 32 participants) in Fallis et al.s' study of upper body forced air warming and 37.5°C (SD: 0.4°C) in the control group (of 29 participants) (Fallis, et al., 2006), which was stated to be a non-significant statistical difference although no p-value was reported. Horn's study of upper body forced air prewarming (Horn, et al., 2002), in contrast, did find a statistically and clinically significant higher

newborn rectal temperature for the warmed air group (37.1°C, SD: +/-0.5°C) versus 36.2°C, SD: +/-0.6°C for the control group, p<0.001).

Forced air intraoperative warming (upper body or under body) did not therefore significantly improve newborn temperature at birth, but upper body forced air prewarming was found to have a positive effect.

Summary

Forced air warming is effective at improving maternal temperatures, particularly if applied preoperatively. Similarly, preoperative warming was found to have an increase in almost 1°C (0.9°C) in mean neonatal rectal temperature at birth whereas intraoperative warming did not. Under-body warming appears to have a positive effect on maternal temperature. Preoperative forced air warming was also found to reduce shivering. Results were inconclusive on the effects of forced air and underbody warming on maternal thermal comfort, Apgar scores and umbilical pH.

Leg wrapping

Overview of study

One study (Sun, et al., 2004) compared leg wrapping with tight elastic bandages with leg wrapping with loose elastic bandages in women undergoing elective CS surgery under epidural anaesthesia, with 30 participants in each group. The primary outcome was the effect of the intervention on hypotension (a common occurrence during epidural anaesthesia) but reduction of hypothermia and shivering were secondary outcomes.

Leg wrapping is reported as being applied before administration of the epidural but after the attachment of monitoring, preload of unwarmed fluids and the elevation of the patient's legs to 45° (which seems unlikely given the practicalities of administering the epidural).

Leg wrapping and maintenance of maternal temperature

Maternal sublingual temperature was recorded in the right or left posterior sublingual pocket every three minutes (Sun, et al., 2004) (using a Datex Cardiocap II CG series probe) but was only recorded at five 'observation times': baseline, immediately after epidural anaesthesia, at abdominal skin disinfection, at skin incision and at delivery. Temperature results were only provided for two observation times: at baseline and at delivery (36.5°C, SD: +/- 0.4°C at delivery in the tightly wrapped group versus 36.4°C, SD: +/- 0.3°C in the loosely wrapped group) with the average reduction from baseline to delivery also given (0.4°C, SD: 0.2°C in the tightly wrapped group versus 0.5°C, SD: 0.3°C in the loosely wrapped group). There was no significant difference in temperature between the two groups at these time points and for each group (no p-values reported). Data for the other time points were not presented in an extractable form but we are told that no significant differences existed between the groups for temperature at these time points. Leg wrapping, therefore, presents no benefits in terms of maintenance of maternal temperature, based on evidence from this single study.

Leg wrapping and prevention of shivering

Shivering was measured by an observer, blinded to group assignment, and simply assessed as being either present or absent. There was no difference in the presence of shivering between the groups (21/30 participants shivered in both the tight leg wrapping and also the loose leg wrapping group, p= 0.61) (Sun, et al., 2004). Data for this outcome, as with hypothermia, was only collected until immediately following delivery. As with maternal temperature, leg wrapping is therefore not effective at preventing shivering in this population, based on evidence from this single study.

Leg wrapping and other outcomes

Thermal comfort, time to discharge from PACU, Apgar score, umbilical pH and neonatal temperature were not included as outcomes of interest in this leg wrapping study (Sun, et al., 2004).

Summary

Leg wrapping was therefore not effective at improving maternal temperature or shivering; however, these observations are derived from a single study and therefore should be considered with caution.

Discussion

Perioperative hypothermia is a common occurrence during all types of surgery including CS surgery. Guidance for clinicians in regard to prevention and management of IPH in adult patients is available (NCCNSC 2008) but pregnant patients are excluded from these guidelines. There has been a call for clear guidance to be formulated for CS patients (Chakladar & Harper, 2010), or at least an extension of the current NICE guidelines (NCCNSC 2008) to cover this patient group as perioperative hypothermia can be a disruptive and unpleasant experience for women undergoing CS. Furthermore IPH is associated with numerous undesirable adverse clinical side effects, such as increased blood loss (Rajagopalan, et al., 2008) and delayed wound healing (Kurz, et al., 1996) and is, in most cases, avoidable with careful prevention and management strategies. Utilization of strategies to reduce hypothermia incidence and related adverse effects will also enhance the experience of women having their babies by CS, reducing interference with the time when bonding and breastfeeding can commence. Discussion of these strategies will follow an explanation of the limitations experienced during the systematic review process.

This review includes 12 RCT studies in three broad categories of interventions within the specific population of women undergoing CS. Methodological study issues, such as variations in intervention design and key differences in outcome measurements limited synthesis by meta-analysis. In addition, the reporting of data in graphs and/or figures only meant that extractable data was, in some cases, limited, particularly when authors were largely not contactable. Wide variation in the methods of outcome measurement presented difficulties in the analysis of findings and restricted the meta-analysis undertaken. Temperature was measured at baseline in all studies, but thereafter intervals between measurements and end points of measurement differed. In addition, data was commonly reported for only a limited

number of measurement points, restricting the amount of data available across studies for common time points. There was limited comparability of control groups with very few studies being sufficiently homogenous for meta-analysis, which reduces the strength of determining the benefits of one intervention over another. The wide but subtle variations in treatments also impacted on the heterogeneity of studies.

Wide variations in temperature measurement existed between studies with most methods used as a predictor of core temperature considered for inclusion. Skin temperature measurements were, however, excluded, as peripheral temperature was not an outcome of interest in this review. There are questions about the reliability and accuracy of the wide range of devices and routes used to measure or estimate 'core' temperature, but it is beyond the scope of this review. Consistency within studies of the route for measuring core temperature was considered as vital and an indicator of the quality of outcome measurements.

Visual analogue scales (VAS) or numerical rating scales were used to measure thermal comfort but there was a variety of shivering scales used, albeit similar in nature of descriptors. The assessment of shivering relied largely on the subjective assessment of the (often unblinded) observers. The reliability of the scales used was not addressed – no scale used appears to have been cross-validated.

There were also variations in hypothermia definition evident between studies, despite increasing guidance (NCCNSC 2008) (Association of Operating Room Nurses ARP Committee, 2007; Hooper, et al., 2010) that core temperatures below 36°C should be considered as hypothermic in perioperative patients and treated accordingly. In this review, variations in hypothermia cut-off temperature did not cause difficulties as studies tended to report on temperature decline rather than overall incidence of IPH/core temperatures <36°C. In fact, only one study reported on incidences of IPH (core temperature <36°C) (Chakladar, et al., 2012), and one other study (Smith, et al., 2000) _ENREF_48of IV fluid warming reported on both final intraoperative core temperatures at <35.5°C and <36°C. As the indicator of temperatures <36°C being considered hypothermic becomes more widely accepted and incorporated into practice guidelines on a wider scale, its usefulness in clinical studies will increase.

Insufficient studies utilizing each mode of anaesthesia for each intervention group were included in this review to enable us to identify which interventions were most

effective for use with the different anaesthetic modes (as per the review question). Heat loss during neuraxial anaesthesia, although not subject to the same degree of redistribution as in general anaesthesia, is aggravated by the loss of behavioural thermal regulation below the level of the block and also the lack of a heat loss plateau during longer procedures (as is reached during general anaesthesia). The protective mechanism of shivering is also ablated below the level of block (Saito, et al., 1998). Spinal anaesthesia may have an increased thermoregulatory effect in comparison to epidural anaesthesia (Saito, et al., 1998).

It is clear from the results that forced air warming was less effective where participants received spinal (intrathecal) morphine (Fallis, et al., 2006) (see Table 5), which is thought to be one of the factors contributing to intraoperative hypothermia by altering thermoregulatory thresholds after cephalic spread (Kosai, et al., 1992). Case reports (Hess, et al., 2005; Kosai, et al., 1992),(Ryan, et al., 2012) and one observational study (Hess, et al., 2005) describe a manifestation of hypothermia, presumed related to intrathecal morphine, which tends to be prolonged, accompanied by paradoxical side effects and unresponsive to conventional forced air warming methods (Hess, et al., 2005). Addition of intrathecal opioids, in particular morphine, may have influenced the degree and incidence of hypothermia and therefore the effectiveness of interventions included in this review, as demonstrated by the decreased effectiveness of forced air warming where intrathecal morphine was used. The use or non-use of opioids is not clear in all studies therefore limiting the analysis of this issue in relation to the effectiveness of warming interventions. In order to expand knowledge of the influence of intrathecal opioids on perioperative hypothermia and interventions to treat the condition, further studies specifically investigating this area are required.

Although it is known that the temperature status of both mother and newborn are related, the clinical benefit of warming mothers in relation to newborn outcomes is not clear. Populations studied were similar in terms of gestation, age and excluded conditions. Horn et al.'s study of pre- and intraoperative warming (Horn, et al., 2002) versus unwarmed cotton blankets resulted in the most positive neonatal outcomes in regards to umbilical pH and rectal temperature, although reasons for this are unclear. Chung et al. suggest that the short prewarming period of 15 minutes in their study was insufficient to affect neonatal outcomes (Chung, et al., 2012). Some conflicting

results were found in relation to neonatal outcomes from IV fluid warming: while one study found IV fluid warming increased both Apgar at one minute and umbilical pH (Yokoyama, et al., 2009), another study did not (Chung, et al., 2012). Only one IV fluid warming study measured rectal temperature at birth (Yokoyama, et al., 2009), and this study measured temperature after five minutes, during which time the newborn had been placed under a warmer. While the disparity in neonatal outcomes between existing studies can be considered in relation to study variations, further studies of key neonatal outcomes and maternal warming are required to make more substantive conclusions about clinical benefits to neonates.

Shivering is commonly experienced during CS surgery performed under neuraxial anaesthesia. Findings from this review indicate that intravenous fluid warming and preoperative forced air warming have a role to play in shivering prevention. Pharmacological therapies, which may be used for shivering, were beyond the scope of this review. Shivering is a complex multifactorial (Chan, et al., 1989) phenomenon and not purely thermoregulatory in all instances. Possible explanations for shivering have been described: thermoregulatory shivering triggered by core hypothermia (Sessler, 2008), shivering as a response to fever development (Sessler, 2008), shivering due to local anaesthetic injection stimulation of cold receptors (Chan, et al., 1989; Sessler, 2008) and finally, shivering due to tremulous muscular activity that is in fact non-thermoregulatory. Intrathecal drugs may also contribute to the development of shivering (Woolnough, Allam, et al., 2009).

Findings that warmed IV fluids are effective in maintaining normothermia and reducing shivering are consistent with a previously conducted systematic review of a broad population (Moola & Lockwood, 2011) and support guidance provided by the NICE guidelines (NCCNSC 2008) that have so far applied to only non-pregnant patients. NICE guidelines support the warming of fluids to 37°C for volumes of 500mls and above (NCCNSC 2008). All but one (Chan, et al., 1989) of the included fluid warming studies warmed fluids to 37°C or above. The one study that warmed fluids to a lower temperature of 36.5°C still found that heat loss was reduced in the warmed group; however this group also received extra interventions in the form of warmed preparation fluids and extra clothing (Chan, et al., 1989).

A variety of methods of warming IV fluids were used in the included studies – this review does not make a recommendation of one method of warming the fluids over

another. Woolnough et al. compared Hotline™ warmed fluids with fluids prewarmed in a warming cabinet and recommended that both modes of fluid warming were as efficient (Woolnough, Allam, et al., 2009). Due to ongoing cost considerations, however, they did favour the use of warming cabinets. The use of warmed IV fluids should be standard practice for maintaining normothermia for patients undergoing CS, are easy to administer and do not appear to cause practical concerns for patients and caregivers.

The effectiveness of preoperative warming strategies for women undergoing CS, in particular forced air warming, is confirmed by the results of this review. Again, this recommendation had previously only been provided for either general population groups (Moola & Lockwood, 2011) or non-pregnant patients (NCCNSC 2008). Concerns about whether forced air warming would be practical and tolerable for pregnant patients were not widespread within the included studies, although issues of ability to tolerate active warming were found by one upper body warming study. One participant in the Fallis et al.'s study commenced on a lower temperature setting before increasing it; however, 14 of 32 patients in the intervention group also later adjusted the temperature to a lower setting (Fallis, et al., 2006). Forced air warmers are generally designed to progress to a lower setting automatically after a certain period if the highest setting is chosen. Therefore, the reduction in the temperature setting in Fallis et al.'s study (Fallis, et al., 2006) does not appear to be extraordinary. Fallis et al. also found that thermal comfort was enhanced by active warming (Fallis, et al., 2006), perhaps suggesting that the reduction in the operating temperature of the device does not signify widespread warming related thermal discomfort.

Issues regarding forced air warming for women undergoing CS have been raised by clinicians (Chakladar, et al., 2011). Forced air warming blankets tend to be bulky and the presence of an upper body warming blanket may present difficulties for both women and clinicians especially after delivery of the baby, when women often want to hold and be with their newborn (Chakladar, et al., 2011). Concerns regarding practicality have been raised in the literature (Chakladar, et al., 2011; Chakladar & Harper, 2010; Chan, et al., 1989) but were not raised in the forced air warming studies included in this review. These concerns may be addressed by the utilization of active under-body or lower body warming – unfortunately no study of lower body warming was found to be of sufficient quality for inclusion in the review. Under-

body warming mattresses warm a greater surface area of the body than partial (upper or lower) body warming blankets. In regard to tolerability of under-body warming, the only issue reported by Chakladar et al. (Chakladar, et al., 2012) was the discontinuation of warming for one patient (out of 58 participants in the intervention group) who found the intervention too hot. Additional studies on the effectiveness of carbon polymer mattresses would be beneficial, particularly in comparison to forced air warming mattresses. For this review, the two studies were grouped together as under-body warming and no distinction made as to the particular device employed. Despite the moderate heterogeneity displayed in the meta-analysis, it does appear that under-body warming mattresses (both carbon polymer and forced air warming) are effective for maintaining perioperative temperature, thereby resulting in an increased postoperative temperature and reduced incidence of IPH.

Practical difficulties surrounding the use of upper body forced air warming during surgery may also be partially addressed by the utilization of preoperative forced air warming. Preoperative warming also presents clinical value in reducing intraoperative heat loss and, even relatively short periods such as those utilized by the included studies, may be cost-effective, especially if utilizing resources already in place. Preoperative forced air warming increases peripheral heat content, therefore the core-periphery temperature gradient (which contributes to heat loss during anaesthesia) is decreased (Leslie & Sessler, 2003). Horn et al. emphasize that warming prior to epidural insertion precedes the vasodilation that follows epidural anaesthesia, and contributes to hypothermia (Horn, et al., 2002). The relatively short phase of prewarming used in the included studies, which clinically is probably most achievable, will result in this raising of peripheral temperature. Although prewarming shows real clinical benefits, its feasibility and implementation in practice does depend heavily on the model of care practised, and additional resources required by different institutions, which may present a barrier to implementation. Where possible, preoperative warming should be implemented to protect against intraoperative heat loss.

The overall effectiveness of intraoperative, as opposed to preoperative, upper body forced air warming is less clear. Horn et al. utilised both preoperative and intraoperative warming and found this combination to be effective (Horn, et al., 2002). Fallis et al. utilized only intraoperative warming and found that neither the

control (warmed cotton blankets) nor the intervention group maintained normothermia (Fallis, et al., 2006). The role of intrathecal opioids administered in this study may have influenced these results as discussed earlier. Additional studies on intraoperative warming, both with and without intrathecal opioids, are warranted in this population.

Thermal comfort should also be considered in the context of ambient temperature. Operating theatres are generally cool environments, in accordance with clinical guidelines to this effect – for example, in Australia, Australian College of Operating Room Nurses (ACORN) standards guide operating room temperatures to be between 20-22°C, although provision is made that in certain circumstances, such as for obstetric patients, variations in ambient temperature may be necessary (Australian College of Operating Room Nurses 2012.). The American Society of PeriAnesthesia Nurses (ASPAN) clinical practice guidelines for the promotion of normothermia state that ambient operating room temperatures should be between 20-25°C (Hooper, et al., 2010) while NICE guidelines state that ambient temperatures should be over 21°C while patients are exposed, and can be reduced once the active warming commences (NCCNSC 2008). Ambient temperature was generally above 22°C for the majority of studies included in this review. The degree of comfort derived from an active warming intervention may be greater if the commencing ambient temperature is lower, as may be evident in the contrasting results seen between Fallis et al. and Horn et al.'s studies (Fallis, et al., 2006; Horn, et al., 2002). Participants in Fallis et al.'s study (Fallis, et al., 2006) were subject to an initially cooler ambient temperature in contrast to those in Horn et al.'s study (Horn, et al., 2002) where the ambient temperature was higher. Those in the cooler initial environment had a significant increase in thermal comfort scores (Fallis, et al., 2006), whereas those in the warmer environment did not significantly increase thermal comfort (Horn, et al., 2002). Ambient operating room temperature also increased in the forced air warming group in Fallis et al.'s study (Fallis, et al., 2006), and the authors highlight this as a possible contributing factor to higher thermal comfort scores in this group. Ambient temperature was insufficiently reported in some studies but it is also particularly relevant to the administration of room temperature fluids. Unfortunately, one study that utilized room temperature fluids neglected to provide details of ambient temperature for any of the study groups (Chung, et al., 2012), therefore omitting any

indication of the administration temperature of the room temperature fluids. Details of oxytocin administration would also be useful when assessing thermal comfort score results: as Woolnough et al. discuss, this drug may alter perceptions of warmth due to its tendency to cause facial flushing (Woolnough, Allam, et al., 2009).

Although their study included elective patients only, Horn et al. recommend active warming strategies for emergency CS surgery (Horn, et al., 2002). The majority of patients included in this review underwent elective surgery and therefore the findings are largely applicable to this group. However the application of some warming strategies supported by this review, for example forced air prewarming, may be less practical in true emergency CS situations, with IV fluid warming or even under-body warming being easier to initiate. Chakladar et al. suggest that under-body warming mattresses may make clinical differences for this group, and reduce preparation time as they can be already in place on the operating table ready for use (Chakladar, et al., 2012). The clinical need for hypothermia prevention in emergency cases needs to be individually assessed. Emergency CS patients may be more likely to experience increased blood loss (Chakladar, et al., 2012), intraoperative and postoperative complications, but as with all patients, maternal pyrexia and/or existence of a labouring period prior to CS would need to be considered. Therefore, knowledge of appropriate and effective strategies to maintain thermal balance in this population would be valuable and therefore more research on this is required.

Conclusion

Preoperative warming interventions tend to lead to improved maternal thermoregulatory outcomes in CS surgery. The warming of IV fluids increases intraoperative and postoperative temperatures, whether given as a preload or intraoperatively. Upper body forced air warming applied in the preoperative phase achieves better maintenance of temperature than if applied only during the intraoperative phase. There is also evidence to suggest that under-body warming mattresses are effective at maintaining normothermia, having been shown to be effective at increasing postoperative temperatures on arrival to PACU.

Whether interventions to maintain temperature status in women undergoing CS also improve thermal comfort is less clear, which may depend on a number of factors,

including ambient temperature and the setting of the warming device in question. Both warmed IV fluids and forced air warming interventions (applied preoperatively) have a positive effect on reducing shivering. IV fluid warming is ineffective at improving neonatal temperatures but its effect on Apgar and umbilical pH remains unclear. The use of forced air warming is not effective at improving Apgar scores, but if applied preoperatively appears to be effective at improving newborn rectal temperatures. The effectiveness of forced air warming in improving umbilical pH remains unclear. Findings from this systematic review, in relation to IV fluid warming and preoperative forced air warming, confirm that recommendations made for general adult groups may be applied to the population of women undergoing CS surgery under neuraxial anaesthesia.

Limitations

The included studies in this review predominantly included patients undergoing elective CS surgery, which may limit applicability of the results to those undergoing emergency CS surgery. Studies were mainly small scale and of medium to low quality. Meta-analysis was limited due to the clinical heterogeneity of the included studies. Analysis of intraoperative temperature status was limited due to the many variations in temperature reporting points utilized by the studies. Exploration of the influence of anaesthesia mode on the effectiveness of intervention was also limited due to the lack of studies within each intervention relating to each mode of anaesthesia.

Differences between the review and the published protocol

The review also deviated from the published protocol in relation to exclusion of pharmacological studies. Pharmacological studies that aimed to reduce shivering and that included temperature only as a secondary outcome were identified but their inclusion in the review would have been problematic, as shivering is a complex phenomenon with multiple causes. A review focusing on pharmacological shivering interventions for this population would be an appropriate method to assess this further, as would an exploration of the 'multifactorial' (Chan, et al., 1989) aspects of shivering in this population.

Implications for practice

- Preoperative warming strategies should be utilized where possible (Level 2).
- Preoperative and/or intraoperative warmed IV fluids should be standard practice for women undergoing CS surgery (Level 1).
- Upper body forced air warming should be utilized pre operatively (Level 2).
- Under-body warming mattresses should be used during CS surgery (Level 1).
- Additional strategies, such as the maintenance of ambient temperature, should be used to maintain thermal comfort (Level 2).
- Warming strategies have less effect when intrathecal opioids are administered (Level 2).

Recommendations for practice are based on the JBI Levels of Evidence (JBI) as detailed in Appendix VIII.

Implications for research

- Research is needed to investigate the effectiveness of interventions in emergency CS surgery. Effective and appropriate interventions for protecting thermal balance in these patients may be especially important.
- Investigation into the influence of anaesthetic mode and influence of intrathecal opioids on the incidence of hypothermia and effectiveness of warming interventions would be beneficial. The effectiveness of warming interventions may be altered where intrathecal opioids have been administered, or where hypothermia is related to intrathecal opioids.
- Further investigation into maternal warming and neonatal outcomes would be beneficial as potential benefits for neonates remain unclear.
- Studies on the effectiveness and efficacy of lower body in comparison to upper body forced air warming devices are required: lower body warming may

have reduced practical difficulties for this population, whilst retaining effective heat maintenance but research is needed to confirm this.

- Further study of the use of under-body warming mattresses (carbon polymer versus forced air warming) is required.
- Larger scale studies of warming interventions using standardized and clinically meaningful temperature measurement time points are required, thus facilitating analysis and comparisons of effectiveness of these interventions.

Conflict of Interest

No potential conflicts of interest are identified.

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Appendix B

Systematic Review Critical Appraisal Form

(JBI-MAStARI appraisal instrument)

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

Appendix C

Systematic Review Search Strategy

CINAHL (via EBSCO) 02/05/12

Limits: Human

1. 'C#esarean'
2. MM 'Cesarean Section'
3. MH 'Delivery+'
4. 'parturient'
5. 'parturition'
6. 'maternity'
7. 'maternal'
8. MH 'Obstetrics'
9. MH ' Obstetric Patients'
10. MH 'Surgery, Obstetrical+'
11. MH 'Pregnancy Outcomes'
12. MH ' Anesthesia, Obstetrical'
13. MH 'Obstetric Care'
14. MH 'Obstetric Nursing'
15. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. 'temperature'
17. MH 'Body Temperature Regulation+'
18. MH 'Body Temperature Changes+'
19. MH 'Body Temperature+'
20. MH 'Core Body Temperature+'
21. 'thermoregulation'
22. 'hypothermi*'
23. MH 'Hypothermia'
24. 'shivering'
25. MH 'Shivering'
26. MM 'Thermogenesis'
27. 'heat loss'
28. MH 'Heat Loss'
29. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28
30. 'warm'

31. MH ‘Warming Techniques’
32. ‘active warm*’
33. ‘passive warm*’
34. ‘prewarm*’
35. ‘rewarm*’
36. ‘forced air warm*’
37. ‘heat*’
38. MH ‘Heat’
39. MH ‘Heating’
40. MH ‘Fluid Therapy+/UT’
41. 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40
42. 15 AND 29 AND 41

Embase (via OVID) (30/4/12)

Limits: Human

1. c?esarean.mp
2. MH caesarean section/
3. delivery.mp
4. MH instrumental delivery/
5. c$esarean delivery.mp
6. parturient.mp
7. parturition.mp
8. MH birth/
9. obstetric$.mp
10. MH obstetrics/
11. MH obstetric operation/
12. MH obstetrical nursing/
13. MH pregnancy outcome/
14. MH obstetric anesthesia/
15. matern$.mp
16. MH maternal care/
17. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. temperature.mp

19. MH temperature/
20. MH body temperature/
21. MH body temperature disorder/
22. MH body temperature sensation/
23. MH core temperature/
24. MH skin temperature/
25. MH low temperature/
26. MH hypothermia/
27. MH hypothermi$.mp
28. MH thermoregulation/
29. thermoregulation.mp
30. MH thermogenesis and thermoregulation/
31. thermogenesis.mp
32. MH thermogenesis/
33. MH shivering.mp
34. MH shivering/
35. heat loss.mp
36. MH heat loss/
37. MH cold/
38. MH cold sensation/
39. MH exp accidental hypothermia/su (Surgery)
40. 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39
41. MH warm$.mp
42. MH warming/
43. MH heat/
44. MH heat treatment/
45. heat$.mp
46. prewarm$.mp
47. active warm$.mp
48. passive warm$.mp
49. forced air warm$.mp
50. MH fluid therapy/

51. 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49
52. 17 AND 40 AND 51

Medline (via OVID) (02/05/12)

Limits: Human

1. C?esarean.mp
2. MH Cesarean Section/
3. C?esarean delivery.mp
4. Delivery, Obstetric.mp
5. parturient.mp
6. parturition.mp
7. MH Parturition/
8. MH Obstetrics/
9. obstetric$.mp
10. MH Obstetrical Surgical Procedures/
11. MH Obstetrical Nursing/
12. MH Pregnancy Outcome/
13. MH Anesthesia, Obstetrical/
14. matern$
15. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14
16. MH Body Temperature Regulation/
17. MH Body Temperature/
18. temperature.mp
19. MH Temperature/
20. MH Cold Temperature/
21. hypotherm$.mp
22. MH Hypothermia/
23. thermogenesis.mp
24. MH Thermogenesis/
25. shivering.mp
26. MH Shivering/
27. heat loss.mp
28. thermoregulation.mp

29. 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28
30. warm$.mp
31. MH Hot Temperature/tu, th (Therapeutic Use, Therapy)
32. rewarm$.mp
33. MH Rewarming/
34. prewarm$.mp
35. active warm$.mp
36. passive warm$.mp
37. forced air warm$.mp
38. MH 'Bedding and Linens'/ut (Utilization)
39. heat$.mp
40. MH exp Hypothermia/pc (Prevention and Control)
41. MH Fluid Therapy/ut (Utilization)
42. 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41

15 AND 29 AND 42

Appendix D

Systematic Review Search Results

Search Results

Database	Date	Strategy	Results
CINAHL	02/05/12	See Appendix C	31
Current Contents	14/05/12	*(Cesarean OR Caesarean) AND (hypotherm*OR warm*) excl. vet and zoology*	109
Embase	30/4/12	See Appendix C	268
Medline (via OVID)	02/05/12	See Appendix C	299
Mednar	02/05/12	*(cesarean OR caesarean) AND (hypothermia OR warming) Full text*	932
ProQuest (incl. PQDT)	14/05/12	*C*esarean AND hypotherm* (exclude: animal science, veterinary science, political science, American history, journalism, mass communication, adult education, rhetoric, animals, artificial intelligence, audiology, Canada, Canadian literature, education history, American literature)*	348 (incl.30 from PQDT)
Web of Science 11/05/12	11/05/12	*(hypotherm* OR warm*) (TOPIC) AND (cesarean OR caesarean) (TOPIC) excl. zoology and veterinary science*	165
CENTRAL	14/05/12	*C*esarean AND (hypotherm* OR warm*) (Title, Abs, Keywords)*	29
OpenGrey	14/05/12	*(caesarean OR caesarean) AND (hypothermia OR warming)*	0
Scopus	14/05/12	*C*esarean AND (hypotherm* OR warm*) in (TITLE-ABS-KEY-AUTHOR) ANDEXCLUDE(SUBJAREA"AGRI")OREXCLUDE(SUBJAREA"ENGI")*	279
Clinical Trials	14/05/12	*(cesarean OR caesarean) AND (hypothermia OR warming)*	7
Total			**2467**

Appendix E

Systematic Review

Verification of Study Eligibility Form

Systematic Review Verification of Eligibility Form

INCLUSION CRITERIA

AUTHOR AND YEAR
JOURNAL
TITLE
REVIEWER
Population: The study population is women undergoing caesarean section. Yes
Intervention: The study participants received active or passive warming measures to prevent or manage heat loss Yes
Outcome: The primary or secondary outcomes include prevention or reduction of maternal or neonatal heat loss Yes
IF YOU HAVE NOT ANSWERED YES TO ALL OF THE ABOVE QUESTIONS, YOU SHOULD EXCLUDE THE STUDY. IF YOU ANSWERED YES TO ALL, PLEASE CONTINUE.

Appendix F

Systematic Review

Data Extraction Instrument

PREVENTION OF PERIOPERATIVE HYPOTHERMIA FOR WOMEN UNDERGOING CAESAREAN SECTION DATA EXTRACTION TOOL

Record Number

Author

Journal

Year **Reviewer**

Study Method

Setting

Participants

	Group 1	**Group 2**	**Group 3**
Number in group			
Mean age and range			
Category: elective/emergency surgery			
Gestation in weeks			
BMI [1]			
ASA status [2]			
Anaesthetic type			
Drugs administered			
Gravida[3]/Parity[4]			
Singleton/multiple birth			
Excluded participants			
Patients who left the study and why			

Notes

[1] BMI – Body Mass Index

[2] ASA status – American Society of Anesthesiologists status

[3] Gravida – refers to the number of pregnancies (Johnson, 2010)

[4] Parity – refers to the number of deliveries (Kenner & Lott, 2007)

Intervention

Method of warming			
Setting (if applicable)			
Duration of warming			
Fluids (if applicable)			
Volume of fluids administered (if applicable)			
Method of warming fluids			
Temperature setting of fluid warmer			
Duration fluids in warmer			
Method of fluid delivery			
Ambient operating theatre temperature			

Outcome

Mode of temperature measurement			
Baseline/start point of temperature measurement			
Timings of temperature measurement			
Timing of end temperature measurement			
Hypothermia definition/cut off			
Maternal thermal comfort (validated scale?)			
Epidural or spinal block height			
Maternal satisfaction (validated scale?)			
PACU length of stay			
Umbilical pH			
Apgar score			
Newborn core temperature			
Newborn core temperature measured at what interval?			
Method of newborn core temperature measurement			
Other outcomes			

Results

Dichotomous data

Outcome	Treatment group number/total number	Control group number/total number

Continuous data

Outcome	Treatment group mean and SD (number)	Control group mean and SD (number)

Author's conclusions

Reviewer's conclusions

Appendix G

Systematic Review

Included Studies

Author Year	Design	Population			Intervention Comparator	Outcomes		Results/conclusions
		Cat	Anaesth	No		Temperature Mode	Other	
Chakladar 2011	RCT	Elective	Spinal/CSE/ Epidural/GA (opioids)	116	Full body carbon polymer warming mattress switched ON and warmed IV fluids (40°C) vs full body warming mattress switched OFF and warmed IV fluids (40°C)	Incidence of inadvertent perioperative hypothermia(< 36°C) Temporal artery	Mean Hb drop	Incidence of IPH was reduced in the warming mattress group.
Chan 1989	RCT	Elective	Epidural	40	Warmed IV fluids (36.5°C), warmed prep and extra clothing vs room temp fluids, prep and single hospital gown	Mean drop in temperature Bladder, oral	Shivering	Warmed IV fluids, with additional clothing, reduced heat loss but did not reduce the incidence of shivering.
Chung 2012	RCT	Elective	Spinal (no opioids)	45	Warmed IV fluid preload (37-38°C administration temperature) vs upper body forced air prewarming (43°C) with unwarmed IV fluid preload vs unwarmed fluid preload	Core temperature at 45 mins Skin temperature at 15 mins, 30 mins Aural infrared and skin temperature of upper arm and thigh	Maternal thermal comfort, pain, shivering, nausea, umbilical vein pH, Apgar at 1 min, nausea, vomiting.	Both preoperative upper body forced air warming and warmed IV fluids reduced hypothermia and shivering in patients, compared to the control group. Neonatal outcomes were not improved in any group.

Author Year	Design	Population			Intervention Comparator	Outcomes		Results/conclusions
		Cat	Anaesth	No		Temperature Mode	Other	
Fallis 2006	RCT	Elective	Spinal (intrathecal morphine)	62	Upper body forced air warming (43°C) vs warmed cotton blanket	Mean baseline oral temperature decrease throughout procedure Final temperature Oral	Maternal thermal comfort, umbilical pH, Apgar at 1 & 5 minutes, newborn rectal temp at delivery, pain scores, shivering, interventions for hypoglycemia for newborn <3hrs of delivery	Warmed cotton blankets were comparable to upper body forced air warming in relation to body temperature of mothers and newborns. Forced air warming resulted in higher thermal comfort scores at 30 minutes. Authors suggest further research on lower body warming. Warmed cotton blankets suggested as standard care for this population.
Goyal 2011	RCT	Elective	Spinal (no opioids)	64	IV fluids at room temperature (22°C) vs IV fluids from fluid warmer (39°C)	Core temp <36°C on arrival to PACU. Mean baseline core temperature, on arrival to PACU, 30 mins after arrival, mean discharge temp from PACU. Aural infrared	Time to discharge from PACU, shivering	IV fluid warming resulted in less core temperature drop than room temperature fluids but was not effective in preventing shivering and reducing time to discharge in PACU.

Author Year	Design	Population			Intervention Comparator	Outcomes		Results/conclusions
		Cat	Anaesthetic	No		Temperature Mode	Other	
Horn 2002	RCT	Elective	Epidural	30	Preoperative and intraoperative upper body forced air warming (43°C) preoperatively vs single cotton blanket	Final intraoperative core temperature Tympanic thermocouple	Maternal thermal comfort, pain umbilical vein pH, newborn rectal temp, shivering	Preoperative upper body forced air warming reduced core temperature heat loss and maternal shivering, and improved umbilical vein pH Period of 15 minutes prewarming recommended for this population.
Oshvandi 2011	RCT	Elective	General	62	Warmed IV fluids (37°C) vs room temperature (25°C) fluids (pre surgery)	Average temp at the end of anaesthesia Aural infrared	Shivering, pethidine intake	Preoperative administration of warmed fluids improved postoperative core temperature and reduced shivering in the intervention group.
Reidy 2008	RCT	Elective or 'semi-urgent'	Spinal or spinal-epidural (intrathecal opioids)	68	Under body forced air warming blanket vs 'standard care'	Baseline temperature and temperature on entering PACU Oral	Maternal thermal comfort, umbilical pH, Apgar at 1 and 5 mins, newborn axillary temp 1 minute delivery, surgeon's thermal comfort scores	Full under body forced air warming resulted in warmer maternal temperatures but did not improve maternal thermal comfort.

Author Year	Design	Population			Intervention Comparator	Outcomes		Results/conclusions
		Cat	Anaesth	No		Temperature Mode	Other	
Smith 2000	RCT	Elective	Spinal or epidural	67	Warmed IV fluids via Hotline (42°C set point) vs room temp fluids (20-22°C)	Final core <36 °C, final core <35.5°C, core temp decrease after induction of regional anaesthesia, core baseline temperature, core lowest temperature, core final temp, core change (lowest – baseline) Change range (core lowest-baseline), core change (final-baseline), change range (core final – baseline), PACU core temp on arrival, PACU core temp after 30 mins, PACU core temp after 60mins PACU at discharge Tympanic thermocouple	Shivering, number of interventions to treat hypothermia	Patients in the warmed IV fluids group experienced a lesser core temperature decrease to those in the control group but did not experience decreased incidence of shivering or time to discharge in PACU. A combined approach to warming, utilizing fluid warming in conjunction with convective warming is recommended.

Author Year	Design	Population			Intervention Comparator	Outcomes		Results/conclusions
		Cat	Anaesth	No		Temperature Mode	Other	
Sun 2004	RCT	Elective	Epidural	60	Leg wrapping with tight elastic bandages vs leg wrapping with loose elastic bandages	Baseline temp, temp at delivery, average reduction (°C) baseline to delivery Sublingual	Shivering, hypotension, Apgar scores	Leg wrapping with elastic bandages does not prevent hypothermia or shivering in this population.
Woolnough 2009	RCT	Elective	CSE with intrathecal diamorphine	75	Room temp IV fluid preload vs warmed IV fluid preload (warming cabinet) (40-41°C) vs IV fluid preload via Hotline fluid warmer (42°C)	Temp decrease during first 60 mins following CSE Aural infrared	Pain, shivering	A preload of warmed IV fluids reduced maternal temperature decline and improved thermal comfort, but did not reduce shivering. It is suggested that IV fluids should be routinely warmed for all CS patients in line with NICE guidelines for adult (non-pregnant) patients.[6]
Yokoyama 2009	RCT	Elective	Spinal (no opioids)	30	Warmed IV fluids (38°C) and reflective blanket vs unwarmed IV fluids and reflective blanket (25°C)	Temp at baseline, at delivery, 15, 30 and 45 minutes after delivery. Forearm-fingertip temp gradient after spinal administration and at time of incision.	Newborn rectal temp at 5 mins, Apgar scores at 1 and 5 mins, umbilical artery pH, Hb concentration, lowest BP, blood loss	Prewarmed IV fluid administration resulted in higher maternal core temperatures, higher umbilical arterial pH and higher Apgar scores at 1 minute.

Appendix H

Systematic Review

Excluded Studies

Aboud E, Neales K. The effect of maternal hypothermia on the fetal heart rate. International Journal of Gynaecology and Obstetrics. 1999. 66 (2): 163-4

Reason for exclusion: case report, not research

Aglio LS, Johnson MD, Datta S, Ostheimer GW. Warm intravenous fluids reduce shivering in parturients receiving epidural anaesthesia. Anaesthesiology. 1988. 69, 3A

Reason for exclusion: unclear randomisation

Baker B. Maternal hypothermia in scheduled cesarean section births and neonatal outcomes. http://awhonn.confex.com/awhonn/2012/webprogram/Paper8180.html. Access date 09/05/12 (Conference presentation)

Reason for exclusion: retrospective chart review

Baysinger CL. The effect of forced air warming during cesarean section on postoperative infectious morbidity (2008) http://clinicaltrials.gov/ct2/show/NCT00696462. Access date: 14/05/12 (Clinical Trial Protocol)

Reason for exclusion: insufficient information

Berglund A, Bacci A, Blyumina A, Linkmark, G. Successful implementation of evidence-based routines in Ukrainian maternities. Acta Obstetrica et Gynecologica Scandinavica. 2010. 89 (2): 230-7

Reason for exclusion: population and intervention not relevant

Buggy DJ, Gardiner J. The space blanket and shivering during extradural analgesia in labour. Acta Anaesthesiologica Scandinavica. 1995.39 (4): 551-553

Reason for exclusion: Caesarean Section excluded

Burchman CA, Datta S. Ostheimer GW. Delivery temperature of heated intravenous solutions during rapid infusion. Journal of clinical anesthesia. 1989. 1 (4): 259-261

Reason for exclusion: in vitro study

Butwick AJ, Lipman SS, Carvalho B. Intraoperative forced air warming during cesarean delivery under spinal anesthesia does not prevent maternal hypothermia. Anesthesia and Analgesia. 2007. 105 (5): 1413-1419

Reason for exclusion: did not meet quality criteria

Capogna G, Celleno D. Intravenous clonidine for post-epidural shivering in parturients. British Journal of Anaesthesia. 1993. 71 (2): 294-5

Reason for exclusion: intervention not relevant

Capogna G, Celleno D. Improving epidural anesthesia during cesarean section: causes of maternal discomfort or pain during surgery. International Journal of Obstetric Anesthesia. 1994. 3 (3): 149-152

Reason for exclusion: review article

Casey WF, Smith CE, Katz JM, O'Loughlin K, Weeks SK. Intravenous meperidine for control of shivering during Caesarean Section under epidural anaesthesia. Canadian Journal of Anaesthesia. 1988. 35 (2): 128-133

Reason for exclusion: intervention not relevant

Chakladar A, Harper CM. Peri-operative warming in caesarean sections: guidance would be NICE. Anaesthesia. 2010. 65 (2: 212-213

Reason for exclusion: not research

Chen CM. Central to peripheral temperature differences in full-term neonates delivered vaginally and by cesarean section during the first two hours of life. Clinical Neonatology. 2005. 12 (2): 51-54

Reason for exclusion: study population neonates, maternal temperature not recorded

Christensson K. Fathers can effectively achieve heat conservation in healthy newborn infants. Acta Paediatrica, International Journal of Paediatrics. 1996. 85 (11): 1354-1360

Reason for exclusion: study population neonates, maternal temperature not recorded

Clark V, McGrady E, Sugden C, Dickson J, McLeod G. Speed of onset of sensory block for elective extradural Caesarean section: choice of agent and temperature of injectate. British Journal of Anaesthesia. 1994. 72 (2): 221-223

Reason for exclusion: intervention not relevant, outcome not reduction of maternal heat loss

Dale M, Crawford M, Johnston P. Audit of inadvertent perioperative hypothermia in the maternity theatre. Anaesthesia and Intensive Care. 2011. 39 (4): 702

Reason for exclusion: audit

Fardig JA. A comparison of skin-to-skin contact and radiant heaters in promoting neonatal thermoregulation. Journal of Nurse-Midwifery, 1980. 25 (1): 19-28

Reason for exclusion: study population excludes Caesarean Section

Glosten B, Sessler DI, Faure EA, Karl L, Thisted RA. Central temperature changes are poorly perceived during epidural anesthesia. Anesthesiology, 1992. 77 (1): 10-16

Reason for exclusion: randomisation unclear

Gouchon S, Gregori D, Picotto S, Patrucco G, Nangemi M, Di Giulio P. Skin-to-skin contact after cesarean delivery: an experimental study. Nursing Research. 2010. 59(2): 78-84

Reason for exclusion: intervention commences outside of the perioperative setting

Halloran OJ. Warming our Cesarean section patients: why and how? Journal of Clinical Anesthesia. 2009. 21 (4): 239-241

Reason for exclusion: not research article

Harper C.M, Alexander R. Hypothermia and spinal anaesthesia (11). Anaesthesia. 2006. 61 (6): 612

Reason for exclusion: not research article

Hernandez-Bernal CE, Martinez-Sánchez A, Oriol-López SA, Castelazo-Arredondo JA. Tremor y bloqueo peridural en cesárea. Revista Mexicana de Anestesiologia. (2009). 32 (2): 107-113

Reason for exclusion: intervention not relevant

Hess PE, Snowman CE, Wang J. Hypothermia after cesarean delivery and its reversal with lorazepam. International journal of obstetric anesthesia. 2005. 14 (4): 279-283

Reason for exclusion: insufficient information from case series

Hong J-Y, Lee IH. Comparison of the effects of intrathecal morphine and pethidine on shivering after Caesarean delivery under combined spinal epidural anaesthesia. Anaesthesia. 2005. 60: 1168-1172

Reason for exclusion: outcome not reduction of maternal heat loss

Huang Y-Y, Huang C-Y, Lin S-M, Wu S-C.(Effect of very early kangaroo care on extrauterine temperature adaptation in newborn infants with hypothermia problems). Hu Li Tsa Chih - Journal of Nursing. 2006. 53 (4): 41-8

Reason for exclusion: unable to obtain full text article

Huffnagle HJ, Norris MC, Grieco WM, Leighton BL, Arkoosh VA, Huffnagle SL, Glosten B. Hypothermia and shivering during spinal-anesthesia for cesarean delivery. Anesthesiology. 1993. 79 (3A): A1021-1021. (Conference abstract)

Reason for exclusion: randomisation unclear

Hui CK, Huang CH, Lin CJ, Lau HP, Chan WH, Yeh HM. A randomised double-blind controlled study evaluating the hypothermic effect of 150mcg morphine during spinal anaesthesia for Caesarean Section. Anaesthesia. 2006, 29-31

Reason for exclusion: outcome not reduction of maternal heat loss

Jadhon ME, Main EK. Fetal bradycardia associated with maternal hypothermia. Obstetrics and Gynecology. 1988. 72 (3 Pt2): 496-7.

Reason for exclusion: case report. Outcome not reduction of maternal heat loss.

Javaherfaroosh F, Akhondzadeh J, Aein KB, Olapuor A., Samimi M. Effects of tramadol on shivering post spinal anesthesia in elective cesarean section. Pak J Med Sci, 2009. 35 (1): 12-17

Reason for exclusion: Intervention not relevant, temperature data not reported

Johnson MD, Sevarino FB, Lema MJ. Cessation of shivering and hypothermia associated with epidural sufentanil. Anesthesia and Analgesia. 1989. 68 (1): 70-71

Reason for exclusion: case report

Jorgensen JS, Bach LF, Helbo-Hansen HS, Nielsen PA. Warm or cold saline for volume preload before spinal anaesthesia for caesarean section? International Journal of Obstetric Anesthesia. 2000. 9 (10): 20-25

Reason for exclusion: not the right outcome

Jovanovic NC, LoncarStojiljkovic D, Marenovic, T. Prophylaxis and treatment of post-anaesthetic shivering and untoward thermogenesis with tramadol. 9th European Congress on Intensive Care Medicine, ed. D Bennett. 1996: 821-825

Reason for exclusion: study population not women undergoing Caesarean Section

Joy SDS. Skin-to-skin contact after a cesarean and risk of hypothermia. The American Journal of Nursing. 2010. 110 (8): 67

Reason for exclusion: not research

Jung HM, Kim MH. Effects of a warmed blanket for the relieving of cold discomfort after Cesarean Section. Journal of the Korean Academy of Fundamentals in Nursing. 2000. 7 (1): 16-29

Reason for exclusion: appears to be a duplicate of another paper

Kavee EH, Ramanthan S, Bernstein J, Zakowski MI. The hypothermic action of epidural and subarachnoid morphine in parturients. Regional Anesthesia, 1991. 16 (6): 325-328

Reason for exclusion: outcome is degree of heat loss not prevention of heat loss

Kent AL, Williams J. Increasing ambient operating theatre temperature and wrapping in polyethylene improves admission temperature in premature infants. Journal of Paediatrics and Child Health. 2008. 44 (6): 325-331

Reason for exclusion: retrospective chart review

Khan ZH, Zanjani AP, Makarem J, Samadi S. Antishivering effects of two different doses of intrathecal meperidine in caesarean section: a prospective randomised blinded study. European Journal of Anaesthesiology. 2011. 28 (3): 202-206

Reason for exclusion: intervention not relevant

Khezri MB, Bandari AM, Asefzade A, Atlasbaf A. The effect of diclofenac Na suppository on postoperative shivering in patients undergoing elective caesarean section surgery. Pakistan Journal of Medical Science. (2011). 27 (5): 1145-1148

Reason for exclusion: intervention not relevant

Lee S-H.R, Leighton BL, Arkoosh VA, Atkinson PA. A comparison of four warming regimens during cesarean delivery under spinal anesthesia. Anesthesiology, 1997. 87 (3 SUPP): A870

Reason for exclusion: insufficient information regarding methods

Liu WHD, Luxton MC. The effect of prophylactic fentanyl on shivering in elective Caesarean section under epidural anaesthesia. Anaesthesia. 1991. 46: 344-348

Reason for exclusion: intervention not relevant.

Martin H, Norman M. Skin microcirculation before and after local warming in infants delivered vaginally or by caesarean section. Acta Paediatrica, International Journal of Paediatrics. 1997. 86 (3): 261-267

Reason for exclusion: study population not women undergoing Caesarean Section

McCarroll SM, Cartwright P, Weeks SK, Donati F. Warming intravenous fluids and the incidence of shivering during cesarean sections under epidural anesthesia. Canadian Anaesthestists Society Journal. 1986. 33 (3): S72-S73

Reason for exclusion: randomisation unclear

Mitchell JC, D'Angelo M. Implications of hypothermia in procedural areas. Journal of Radiology Nursing. 2008. 27(2): 70-73

Reason for exclusion: not research

Munn MB, Rouse DJ, Owen J. Intraoperative hypothermia in post-cesarean wound infection. Obstetrics and Gynecology. 1998. 91 (4): 582-584

Reason for exclusion: outcome not reduction of maternal heat loss

Negishi C, Ozaki M, Sessler DI, Matsukawa T, Suzuki H, Ozaki K, Atarashi K. Forced-air warming prevents shivering during cesarean delivery with epidural anesthesia. Anesthesia and Analgesia. 1997. 84: S398

Reason for exclusion: did not meet quality criteria

Negishi C, Ozaki M, Suzuki H, Ohno T. Temperature changes and thermoregulatory responses during epidural anesthesia in women undergoing cesarean delivery. Japanese Journal of Anesthesiology. 1996. 45 (5: 558-564. (Japanese)

Reason for exclusion: outcome not reduction of maternal heat loss

Parsa T, Dabir S, Radpay B. The effect of rapidly infused intravenous room temperature fluids in occurrence of perioperative mild hypothermia. European Journal of Anaesthesiology. 2010. 27 (47): 235

Reason for exclusion: outcome not prevention of hypothermia/ reduction of maternal heat loss

Parsons M, Stott S. Hot Mommas! Pre-Warming of Maternity Patients Undergoing Caesarean Section. 2012.

http://www.awhonn.confex.com/awhonn/2012/webprogram/Paper8562.html. Accessed: 08/05/12. (Conference Abstract)

Reason for exclusion: not research (practice improvement project/audit)

Peillon P, Dounas M, Lebonhomme JJ, Guittard Y. Severe hypothermia associated with cesarean section under spinal anesthesia. Annales Françaises d' Anesthésie et de Réanimation. 2002. 21(4): 299-302

Reason for exclusion: not research (case report)

Petsas A, Vollmer H, Barnes R. Peri-operative warming in Caesarean Sections. Anaesthesia. 2009. 64 (8): 921-922

Reason for exclusion: not research

Ponte J, Collett BJ, Walmsley A. Anaesthetic temperature and shivering in epidural anaesthesia. Acta Anaesthesiologica Scandinavia. 1986. 30(7): 584-7

Reason for exclusion: outcome measurements cease before commencement of surgery

Roy J-D, Girard M, Drolet P. Intrathecal meperidine decreases shivering during caesarean section under spinal anaesthesia. Anaesthesia and Analgesia. 2004. 98 (1): 230-234

Reason for exclusion: does not report data on primary outcome

Ryan KF, Price JW, Warriner CB, Choi PT. Persistent hypothermia after intrathecal morphine: case report and literature review. Canadian Journal of Anaesthesia. 2012. 59 (4): 384-388

Reason for exclusion: study population not women undergoing caesarean section

Saito T, Sessler DI, Fujita K, Ooi Y, Jeffrey R. Thermoregulatory effects of spinal and epidural anesthesia during cesarean delivery. Regional Anesthesia and Pain Medicine. 1998. 23 (4): 418-423

Reason for exclusion: comparing heat loss between different modes of anaesthesia not preventing heat loss

Sayyid SS, Jabbour DG, Baraka AS. Hypothermia and excessive sweating following intrathecal morphine in a parturient undergoing cesarean delivery. Regional Anesthesia and Pain Medicine. 2003. 28 (2): 140-143

Reason for exclusion: not research (case report)

Severino FB, Johnson MD, Lema MJ, Datta S, Ostheimer GW, Naulty JS. The effect of extradural sufentanyl on shivering and body temperature in the parturient. Anaesthesia and Analgesia. 1989, 69: 530-533

Reason for exclusion: outcome development of hypothermia not prevention of hypothermia

Sharkey A, Gulden RH, Lipton JM, Giesecke AH. Effect of radiant heat on the metabolic cost of postoperative shivering. British Journal of Anaesthesia. 1993. 70(4): 449-450

Reason for exclusion: study population not exclusively women undergoing Caesarean Section

Sharkey A, Lipton JM, Murphy MT, Giesecke AH. Inhibition of postanaesthetic shivering with radiant heat. Anesthesiology. 1987. 66: 249-252

Reason for exclusion: study population not exclusively women undergoing Caesarean Section

Shebabi Y, Gatt S, Buckman T, Isert P. Effects of adrenaline, fentanyl and warming of injectate on shivering following extradural analgesia in labour. Anesthesia and Intensive Care. 1990. 18 (1): 31-37

Reason for exclusion: does not meet quality criteria

Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. Indian Journal of Anesthesia. 2011. 55 (3): 242-246

Reason for exclusion: study population does not include women undergoing Caesarean Section

Sims C. Simple method for warming fluids for caesarean section. Anaesthesia and Intensive Care. 1993. 21 (1): 124-125

Reason for exclusion: not research

Sleth JC, Servais R, Saizy C. Hypothermia after spinal anaesthesia: errors in temperature measurement. Annales Françaises d' Anesthésie et de Réanimation. 2006. 25 (6): 661-662. (French)

Reason for exclusion: not research

Sultan P. Temperature study in Cesarean Section. 2010. http://clinicaltrials.gov/ct2/show/NCT01249014 Accessed: 14/05/12. (Clinical Trial protocol)

Reason for exclusion: results not available.

Techanivate A, Rodanant O, Tachawattanawisal W, Somsiri T. Intrathecal fentanyl for prevention of shivering in Cesarean Section. Journal of the Medical Association of Thailand. 2005. 88 (9); 1214-1221

Reason for exclusion: intervention not relevant.

Usman SB, Menon V. Avoiding caesarean section in maternal hypothermia associated with marked fetal distress. Emergency Medicine Journal. 2008. 25 (3): 177

Reason for exclusion: not research

Valente A, Ciano F, Suppa E, Draisci, G. Hypothermia after cesarean section with combined spinal-epidural anesthesia and postoperative epidural analgesia. International Journal of Obstetric Anesthesia. 2008. 17 (1): 78

Reason for exclusion: not research

Vaughans B. Early maternal-infant contact and neonatal thermoregulation. Neonatal Network - Journal of Neonatal Nursing. 1990. 8 (5): 19-21

Reason for exclusion: study population not women undergoing Caesarean Section

Wishaw K, Hypothermia associated with subarachnoid morphine. Anaesthesia and Intensive Care. 1997. 25 (5): 586

Reason for exclusion: not research

Woolnough MJ, Hemingway C, Allam J, Cox M, Yentis SM. Warming of patients during Caesarean section: a telephone survey. Anaesthesia. 2009. 64 (1): 50-53

Reason for exclusion: telephone survey

Workhoven MN. Intravenous fluid temperature, shivering, and the parturient. Anesthesia and Analgesia. 1986. 65 (5): 496-498

Reason for exclusion: does not meet quality criteria

Yentur EA, Topcu I, Ekici Z, Ozturk T, Keles GT, Civi M et al. The effect of epidural and general anesthesia on newborn rectal temperature at elective cesarean section. Brazilian Journal of Medical and Biological Research. 2009. 42 (9: 863-867

Reason for exclusion: study population neonates

Young M. Conference report: Fetal and maternal heat balance. Hamburg May 1989. Placenta, 1990. 11 (1): 91-93

Reason for exclusion: not research

Appendix I

JBI Levels of Evidence

JBI Levels of Evidence (JBI)

Levels of evidence	Feasibility F (1-4)	Appropriateness A (1-4)	Meaningfulness M (1-4)	Effectiveness E (1-4)	Economic evidence
1	Meta-synthesis of research with unequivocal synthesized findings	Meta-synthesis of research with unequivocal synthesized findings	Meta-synthesis of research with unequivocal synthesized findings	Meta-analysis (with homogeneity) of experimental studies (eg RCT with concealed randomisation) OR One or more large experimental studies with narrow confidence intervals	Meta-synthesis (with homogeneity) of evaluations of important alternative interventions comparing all clinically relevant outcomes against appropriate cost measurement, and including a clinically sensible sensitivity analysis
2	Meta-synthesis of research with credible synthesized findings	Meta-synthesis of research with credible synthesized findings	Meta-synthesis of research with credible synthesized findings	One or more smaller RCTs with wider confidence intervals OR Quasi-experimental studies(without randomisation)	Evaluations of important alternative interventions comparing all clinically relevant outcomes against appropriate cost measurement, and including a clinically sensible sensitivity analysis
3	a. Meta-synthesis of text/opinion with credible synthesized findings b. One or more single research studies of high quality	a. Meta-synthesis of text/opinion with credible synthesized findings b. One or more single research studies of high quality	a. Meta-synthesis of text/opinion with credible synthesized findings b. One or more single research studies of high quality	a. Cohort studies (with control group) b. Case-controlled c. Observational studies(without control group)	Evaluations of important alternative interventions comparing a limited number of appropriate cost measurement, without a clinically sensible sensitivity analysis
4	Expert opinion	Expert opinion	Expert opinion	Expert opinion, or physiology bench research, or consensus	Expert opinion, or based on economic theory

Appendix J

Systematic Review Publications

Statements of Contributions

Statement of Contribution of Co-Authors for Thesis by Published Paper

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student's thesis and its publication on the Australasian Research Online database consistent with any limitations set by publisher requirements.

In the case of this chapter:

Munday J, Hines S, Wallace K, Chang AM, Gibbons K, Yates P. *The clinical effectiveness of interventions to assist perioperative temperature management for women undergoing Cesarean Section: a systematic review.* JBI Database of Systematic Reviews and Implementation Reports. 2013. 11 (6): 45-111

Contributor	Statement of contribution*
Student author: Judy Munday Signature: JMunday Date: 22 June 2016	I wrote the protocol, developed the search strategy, conducted critical appraisal, data extraction and analysis, and wrote the discussion, recommendations and final manuscript. I am the principal author based on the International Committee of Medical Journal Editors criteria for authorship.
✓ Co-author: Sonia Hines	Second reviewer assisting with critical appraisal, data extraction, review of protocol, and final manuscript.
✓ Co-author: Karen Wallace	Third reviewer, assisting with critical appraisal, review of protocol and final manuscript.
✓ Co-author: Professor Anne M. Chang	Review of protocol and final manuscript.
✓ Co-author: A/Professor Kristen Gibbons	Review of data analysis and final manuscript.
✓ Co-author: Professor Patsy Yates	Review of final manuscript.

Principal Supervisor Confirmation:
I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.
Name SONYA OSLOVAR Signature Sohare Date 30/6/2016

Statement of Contribution of Co-Authors for Thesis by Published Paper

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student's thesis and its publication on the Australasian Research Online database consistent with any limitations set by publisher requirements.

In the case of this chapter:

Munday J, Hines S, Wallace K, Chang AM, Gibbons K, Yates P. A systematic review of the effectiveness of warming interventions for women undergoing caesarean section. Worldviews on Evidence-based Nursing. 2014. 11 (6) 383-393

Contributor	Statement of contribution*
Student author: Judy Munday Signature: JMunday Date: 22 June 2016	I wrote the protocol, developed the search strategy, conducted critical appraisal, data extraction and analysis, and wrote the discussion, recommendations and final manuscript. I am the principal author based on the International Committee of Medical Journal Editors criteria for authorship.
Co-author: Sonia Hines	Second reviewer assisting with critical appraisal, data extraction, review of protocol, and final manuscript.
Co-author: Karen Wallace	Third reviewer, assisting with critical appraisal, review of protocol and final manuscript.
Co-author: Professor Anne M. Chang	Review of protocol and final manuscript.
Co-author: A/Professor Kristen Gibbons	Review of data analysis and final manuscript.
Co-author: Professor Patsy Yates	Review of final manuscript.

Principal Supervisor Confirmation:
I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name SONYA OSBORNE Signature Sosborne Date 30/6/2016

Appendix K

Retrospective case-control study

Mater Human Research Ethics Committee, Mater Research Governance and Queensland University of Technology Ethics Approvals

Mater

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MATER HEALTH SERVICES HUMAN RESEARCH ETHICS COMMITTEE

27th May 2013

Mrs Judy Munday
Mater Nursing Research Centre
Level 2 Aubigny Place
Raymond Terrace
South Brisbane QLD 4101

Dear Mrs Munday

Re: *Ref №. 2013-32* **Intrathecal morphine related perioperative hypothermia in women undergoing Caesarean Section: an observational study**

I write to advise that the Mater Health Services Human Research Ethics Committee has reviewed this research project on 27th May 2013 and recognise that the project meets the requirement for Low and Negligible Risk Research as set out in the National Statement (Section 5.1.18 – 5.1.21) and has granted ethical approval for your research project. Please accept our very best wishes for the success of this research project. *In all future correspondence with the Research Ethics and Governance Office please quote the Mater reference number.*

Documents reviewed and approved include:

Document	Date
Mater Cover Sheet	22nd Mar 2013
LNR Application Form	20th Mar 2013
Research Proposal	24th Feb 2012
Data Collection Form: Intrathecal morphine and hypothermia observational study	Mar 2013
Judy Munday CV	Mar 2013

This approval is valid until 27th May 2016. Please note the following conditions of approval.

- The Principal Investigator has responsibility for ensuring that the project is conducted in accordance with the National Statement, with relevant legislation and with Mater Health Services and responsibility for monitoring compliance rests with your Head of Department.
- Any departure from the protocol detailed in your proposal must be reported immediately to the Human Research Ethics Committee.
- When you propose a change to an approved protocol, which you consider to be minor, you are required to submit a written request for approval to the Chairperson, through the Research Ethics and Governance Office. Such requests will

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research (2007). The processes used by this HREC to review multi-centre research proposals have been certified by the National Health and Medical Research Council.

Mater Research HREC Office
Room 270 Level 2 Aubigny Place Ph: 07 3163 1585 Fax: 07 3163 2278 Email: research.ethics@mmri.mater.org.au

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Queensland 4101 Australia
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11/07

be considered on a case by case basis and interim approval may be granted subject to ratification at the next meeting of the Human Research Ethics Committee.

- Where substantial changes to any approved protocol are proposed, you are required to submit a full, new proposal for consideration by the Human Research Ethics Committee.
- You are required to advise the Research Ethics Coordinator immediately of any complaints made, or expressions of concern raised, in relation to the study, or if any serious or unexpected adverse events occur.
- To access medical records, for the purpose of this study, please provide a copy of this approval letter to the Health Information Services and Privacy Office (if applicable).
- The Research Ethics and Governance Office may choose to conduct an interim audit of your research project.

You are reminded that this letter constitutes ethical approval only. You must not commence this research project until authorisation from the Research Governance Office has been obtained.

Yours sincerely

A/Prof Andrew Crowden
Chairperson
Mater Health Services Human Research Ethics Committee

QUT Administrative Ethics Approval

Dear Mrs Judy Munday

Project Title: Intrathecal morphine related perioperative hypothermia in women undergoing Caesarean Section: An observational study

Ethics category: Human - Administrative Review

QUT approval number: 1300000365 (Mater Health Services HREC approval number: 2013-32)

QUT clearance until: 27/05/2016 (as per Mater Health Services HREC approval) We are pleased to advise that your administrative review application has been reviewed by the Chair, University Human Research Ethics Committee (UHREC), and confirmed as meeting the requirements of the National Statement on Ethical Conduct in Human Research (2007).

I can therefore confirm that your application has received QUT administrative review approval based on the approval gained from Mater Health Services Human Research Ethics Committee (HREC), approval number 2013-32. We note this HREC has awarded the project ethical clearance until 27/05/2016.

CONDITIONS OF APPROVAL

Please ensure you and all other team members read through and understand all UHREC conditions of approval prior to commencing any data collection:

- Standard: Please see attached or www.research.qut.edu.au/ethics/humans/stdconditions.jsp
- Specific: None apply

Projects approved through an external organisation may be subject to that organisation's review arrangements. Researchers must immediately notify the Research Ethics Unit if their project is selected for investigation / review by an external organisation.

VARIATIONS

Mater Health Services HREC should be considered the lead HREC in terms of the ethical review of this project. As such, all variations must first be approved by Mater Health Services HREC before submission to QUT for ratification. Please submit to QUT using our online variation form: www.research.qut.edu.au/ethics/humans/var/

MONITORING

Please ensure you also provide QUT with a copy of each adverse event report and progress report submitted to Mater Health Services HREC.

Administrative review decisions are subject to ratification at the next available UHREC meeting. You will only be contacted again in relation to this matter if UHREC raises additional questions or concerns.

Please don't hesitate to contact us if you have any queries.

We wish you all the best with your research

Kind regards

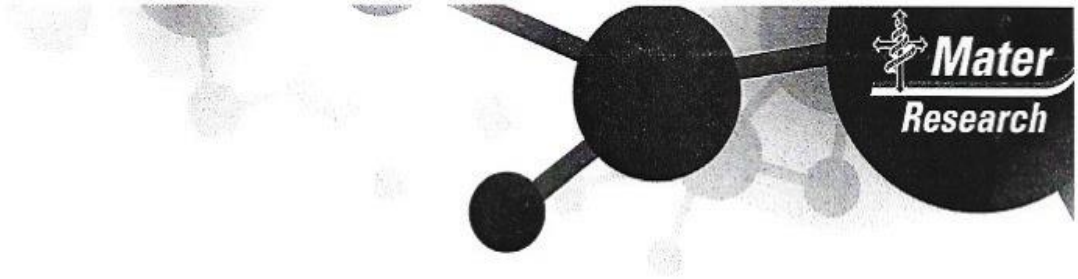
Janette Lamb on behalf of the Chair UHREC

Research Ethics Unit | Office of Research | Level 4 88 Musk Avenue

Kelvin Grove | Queensland University of Technology

p: +61 7 3138 5123 | e: ethicscontact@qut.edu.au | w:

www.research.qut.edu.au/ethics/



MHS & MMRI Human Research Governance - SSA Authorisation

29th May, 2013

Mrs Judith Munday
Mater Nursing Research Centre,
Mater Health Services
South Brisbane, QLD 4101

Dear Mrs Munday

Re: HREC Protocol Ref N°. 2013_32 Intrathecal morphine-related perioperative hypothermia in women undergoing Caesarean Section: an observational study.

Thank you for submitting an application for authorisation of this project. I am pleased to inform you that authorisation has been granted for this study to take place at the following site(s):

Mater Mother's Hospital, South Brisbane

The following conditions apply to this research proposal. These are additional to those conditions imposed by the Human Research Ethics Committee that granted ethical approval.

1. The Research Governance Officer must be informed of any problems that arise during the course of the study which may affect conduct of the study at the site.
2. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project, and which are submitted to the HREC for review, are copied to the research governance officer;
3. Proposed amendments to the research protocol or conduct of the research which only affects the ongoing site acceptability of the project, are to be submitted to the research governance officer;

Head office
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Mercy
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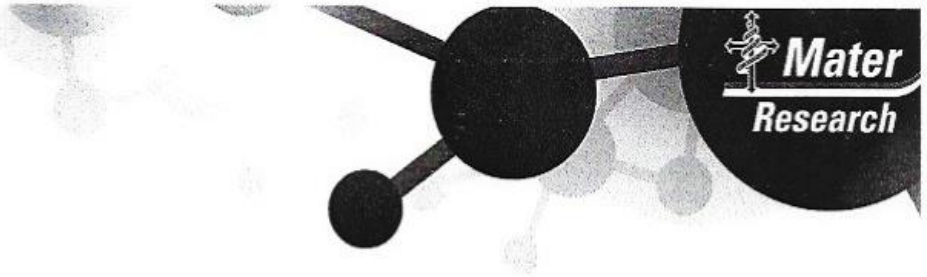
Quality



4. Proposed amendments to the research protocol or conduct of the research which may affect both the ongoing ethical acceptability of the project and the site acceptability of the project are to be submitted to the research governance officer after a HREC decision is made.

We wish you every success in undertaking this research.

Yours sincerely

Patricia Murray, PhD
Research Governance Officer
Room 294, Lvl 2, Aubigny Place
Mater Medical Research Institute
Raymond Terrace
South Brisbane Qld 4101

Ph: (07) 3163 2559
Fax: (07) 3163 1588
Email address: research.governance@mmri.mater.org.au

Appendix L

Retrospective case-control study

Data Collection Tool

DATA COLLECTION FORM ***Intrathecal morphine and hypothermia observational study*** *Date*

Maternal / Demographic details *Identifier No*

Age		Indication for CS	
BMI		Current medication	
ASA score			
Ethnicity			
Parity			
Gravida		Known Adverse Drug Reactions	
Gestation		Maternity history	
Category Select appropriate:	*Emergency*	Past Medical History	
	Elective		
Multiple birth Select appropriate:	*Yes*		
	No		
Drugs in labour (if applicable)			

Perioperative Details

Adm Temp (°C)			In OR suite time		Active warming	Yes / No	
Holding Bay Temp(°C)			Knife to skin time		Type		
					Start time		
Pre op warming	Yes / No		Out OR time		Operating temp of warmer		
Type							
Intra op temp (°C)	Time	Temp	IV fluids Select appropriate	Volume	**Solution/additive**	Warmed (yes/no)	
1			1			Yes	No
2			2			Yes	No
3			3			Yes	No
Temp route			4			Yes	No

Anaesthetic / Intra operative Medication		**Route**	**Time**	**Dose**
Intrathecal Morphine	Yes / No			
Other anaesthetic/ intra operative medication		**Route**	**Time**	**Dose**

Needle type		Level of insertion	
Failure to insert spinal	Yes No	*If yes, details:*	
Inadequate block	Yes No	*If yes details:*	
Reinsertion	Yes No	*If yes, details:*	
High block	Yes No	*If yes details:*	
Other spinal insertion complications			
Intraoperative nausea and vomiting	Yes No	*If yes, details:*	
Intraoperative hypotension	Yes No	*If yes, details:*	
Other complications/ events			

Postoperative Details

PACU Admission time		Patient met all discharge criteria?	Yes No
PACU Ready to discharge time		PACU Discharge Temp	

PACU temp (°C)	Time	Notes / actions
Warming interventions	Yes/No	Notes/Actions
Forced air	Yes No	
Space blanket	Yes No	
Warmed blanket	Yes No	
Overhead heater	Yes No	
Other		

Postoperative Medication In PACU	Route	Time	Dose

Conditions in PACU	**Yes**	**No**	**Additional information**
Shivering			
Nausea			
Vomiting			
Sweating			
Hypotension			
Pruritus			
Haemorrhage			
High spinal block			
Bromage on discharge			

Notes

Appendix M

Retrospective case-control study

Data Collection Guide

Intrathecal morphine and hypothermia data collection: background information

Field	Where/what
Surgery date	On Operation report (purple edge)
Age	On admission report/ work out from patient sticker
BMI	Pre-pregnancy BMI – in orange handheld notes. Also on antenatal summary.
Height/ weight	Pre-pregnancy – in orange handheld notes.
ASA score	On front of anaesthetic chart (purple/white striped edge)
Ethnicity	Antenatal summary
Parity / gravidity/ gestation	Operation report / matrix (birth summary). Parity should include **this** pregnancy.
Category	Operation report
Multiple birth	Operation report / matrix
Indication for CS	Operation report / matrix
Current medication	Anaesthetic chart / medication chart
Allergies	Anaesthetic chart / medication chart
Maternity history	Matrix / operation report / antenatal summary/ anaesthetic chart
Past medical history	Anaesthetic chart / antenatal summary
Drugs in Labour	Matrix / medication chart / labour record
PreOpCheck time	Pre Op checklist (middle column)
In OR suite time / Knife to Skin / End Proc	Operation details (purple edge) - note that Out Proc time is time that procedure ends (**not** the Out OR time at the top of the page)
Pre Op temp / adm temp	Front of anaesthetic chart / last temp on labour record (if labouring) / MET form
Pre Op warming	Pre Op checklist / anaesthetic chart
OT warming / fluid warming	Inside anaesthetic chart
OT temps	Inside anaesthetic chart
IV fluids	Inside anaesthetic chart
Intrathecal morphine?	Inside anaesthetic chart – with details of spinal technique
Other medication incl oxytocics	Inside anaesthetic chart
Spinal needle /level of insertion / failure to insert/ reinsertion/ high block / intraoperative nausea and vomiting	Inside anaesthetic chart
Intraoperative hypotension	Inside anaesthetic chart – see observations. If systolic bp <100mmHg or if <20% from baseline

PACU admission time	On PACU form (see admission to PACU time at top)
Ready to discharge time	On PACU form – see discharge box bottom right side
Discharge criteria met?	On PACU form – see discharge box bottom right side
PACU admission temp	On PACU form – see box on left hand side
PACU discharge temp	On PACU form – see box on left hand side
PACU temps	PACU form
Warming interventions	PACU form – note that Warm Touch often ticked when forced air warming used. Also read notes at bottom of page to see if warming noted there.
PACU medication	PACU form / medication chart
Other conditions in PACU (shivering, hypothermia etc)	This info, if present, will be found in the notes section of the form, which also continues overleaf. May also need to cross-reference with medications given.
Bromage	In notes / observations on PACU form
OT blood loss	Operation report / matrix
PACU blood loss	PACU form / shared handover form

Appendix N

Retrospective case-control study

Statement of Contributions (Accepted paper)

Statement of Contribution of Co-Authors for Thesis by Published Paper

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student's thesis and its publication on the Australasian Research Online database consistent with any limitations set by publisher requirements.

In the case of this chapter:

Munday J, Osborne S, Yates P. Intrathecal morphine related perioperative hypothermia in women undergoing caesarean section: a retrospective case-controlled study. Journal of PeriAnesthesia Nursing (In press)

Contributor	Statement of contribution*
Student author: Judy Munday Signature: JMunday Date: 22 June 2016	Developed the research protocol, and study design, collected data, conducted data analysis, and wrote the final manuscript. I am the principal author based on the International Committee of Medical Journal Editors for authorship.
✓ Co-author: Dr Sonya Osborne	Assisted in development of protocol, aided study design and reviewed final manuscript.
✓ Co-author: Professor Patsy Yates	Assisted in development of protocol, aided study design, and reviewed of final manuscript.

Principal Supervisor Confirmation:
I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name Sonya Osborne Signature Sosborne Date 29/6/2016

Appendix O

Retrospective case-control study

Supplementary Data

Table 2: Demographic and intraoperative variables

Variable	Morphine (n=179): Mean (SD) / number (%)	No Morphine (n=179): Mean (SD) / number (%)
Age (yrs)	30.6 (SD 5.6) (n=178)	30.5 (SD 6.2) (n-178)
Pre-pregnancy BMI	25.4 (SD 6.13) (n =174)	25.7 (SD 5.3) (n=168)
Pre-pregnancy weight (kg)	68.7 (SD 17.8) (n=145)	68.6 (SD 15.5) (n=144)
Height (cm)	162 (SD 7.2) (n=140)	163.3 (SD 7.3) (n=141)
Gestation (days)	264.1 (SD 20.1) (n=177)	265.1 (SD 17.7) (n=179)
Gravidity:	3 (range 1-11) (n = 178)	3 (1-10) (n = 179)
Parity:	2 (range: 1-8) (n = 177)	2 (1-8) (n = 178)
Intraoperative blood loss (mls)	450 (range: 150-2200) (n = 178)	500 (range: 100 – 1300) (n = 174)
Surgical duration (mins): median	41 (n=171)	44 (n=170)
Pre-operative temperature (°C)	36.6 (SD 0.48) (n=155)	36.5 (SD 0.43) (n=137)
Pre-operative waiting time (mins)	36.3 (SD 21.9) (n=170)	37.2 (SD 22.8) (n=163)
Local anaesthetic volume (mls)	2.3 (SD 0.19) (n=172)	2.3 (SD 0.16) (n=165)
Intrathecal fentanyl dose (mcg)		
10mcg	6 (3.4%)	9 (5.3%)
15mcg	139 (78.5%)	84 (49.7%)
20mcg	32 (18.1%)	65 (38.5%)
25mcg	0	11 (6.5%)
Missing	2 (1.1%)	10 (5.6%)
Category: number (%):		
Emergency	82 (46.3%)	85 (47.5%)
Elective	95 (53.7%)	94 (52.5%)
Multiple Birth: number (%):		
Yes	8 (4.5%)	7 (3.9%)
No	168 (95.5%)	172 (96.1%)
ASA: number (%):		
Missing	43 (24.2%)	44 (24.9%)
1	70 (39.3%)	55 (31.1%)
2	55 (30.9%)	64 (36.2%)
3	7 (3.9%)	14 (7.9%)
4	2 (1.1%)	0 (0%)
5	1 (0.6%)	0 (0%)
OT Warming: number (%)		
Missing	154 (86%)	135 (75.8%)
Fluid	16 (8.9%	37 (20.8%)
Forced air	7 (3.9%)	4 (2.2%)
Fluid and forced air	2 (1.1%)	2 (1.1%)
Level of insertion: number (%)		
Missing	45 (25.1%)	45 (25.3%)
L2/L3	9 (5.0%)	8 (4.5%)
L3/L4	107 (59.8%)	96 (53.9%)
L4/L5	18 (10.1%)	28 (15.7%)
L5/S1	0 (0%)	1 (0.6%)
Spinal position (insertion):		
Missing	64 (36%)	57 (32%)
Supine	3 (2 %)	2 (1%)
Lateral	11 (6%)	16 (9%)
Sitting	101 (56%)	104 (58%)

Table 3: Postoperative variables

Variable	Morphine group (n = 179)	No Morphine group (n = 179)
Mean PACU arrival temperature (°C)	35.91 (SD 0.6)	35.88 (SD 0.6)
Mean PACU discharge temperature (°C)	36.25 (SD 0.5) (n = 169)	36.21 (SD 0.48) (n = 162)
Shivering: Yes **No** **Missing**	2 (1%) 176 (98%) 1 (0.5%)	4 (2%) 165 (92%) 10 (6%)
Hypotension (PACU): Yes **No** **Missing**	40 (22%) 136 (76%) 3 (2%)	23 (13%) 154 (86%) 2 (1%)
Nausea: Yes **No** **Missing**	14 (8%) 164 (91.5%) 1 (0.5%)	9 9 (5%) 166 (93%) 4 (2%)
Vomiting: Yes **No** **Missing**	6 (3%) 168 (94%) 5 (3%)	3 (2%) 172 (96%) 4 (2%)
Pruritus: Yes **No** **Missing**	10 (5.5%) 168 (94%) 1 (0.5%)	6 (3%) 169 (94%) 4 (2%)
Haemorrhage: Yes **No** **Missing**	7 (4%) 166 (93%) 6 (3%)	6 (3%) 168 (94%) 5 (3%)
Sweating: Yes **No** **Missing**	3 (2%) 175 (97.5%) 1 (0.5%)	1 (0.5%) 172 (96%) 6 (3%)
PACU duration (mins): median	38.5 (n = 158)	38.5 (n = 162)
Bromage: 0 **1** **2** **3** **Missing**	0 (0%) 2 (1%) 8 (4.5%) 17 (9.5%) 152 (85%)	8 (4.5%) 7 (4%) 15 (8%) 41 (23%) 108 (60.5%)
High Block: Yes **No** **Missing**	3 (2%) 168 (94%) 8 (4.5%)	0 (0%) 166 (94%) 11 (6%)
Postoperative hypothermia (on arrival to PACU): Yes **No** **Missing**	98 (55%) 81 (45%) 0 (0%)	103 (58%) 76 (42%) 0 (0%)
Profound hypothermia: Yes **No** **Missing**	6 (3%) 173 (97%) 0 (0%)	2 (1%) 177 (99%) 0 (0%)

Table 5: Temperature, anaesthetic and surgical variables by year.

Year	Mean preoperative temperature (°C)	Mean postoperative PACU temperature (°C)	Mean intrathecal morphine dose (mcg)	Mean temperature decline (°C)	Mean intrathecal fentanyl dose (mcg)	Median duration of procedure (mins)
2007	36.6 (SD 0.5)	36.0 (SD 0.6)	125 (SD 25.4)	-0.68 (SD 0.69)	16.8 (SD 3.2)	38.5 (n = 66)
2008	36.5 (SD 0.5)	35.7 (SD 0.6)	141.7 (SD 19.2)	- 0.71 (SD 0.8)	16.1 (SD 4.4)	37.5 (n = 32)
2009	36.5 (SD 0.4)	35.6 (SD 0.6)	136.1 (SD 23.0)	-0.80 (SD 0.6)	14.9 (SD 2.6)	41 (n = 33)
2010	36.5 (SD 0.4)	35.9 (SD 0.6)	112.5 (SD 22.1)	- 0.59 (0.6)	16.0 (SD 2.5)	44 (n = 45)
2011	36.6 (SD 0.5)	36.0 (SD 0.6)	119.0 (SD 24.2)	-0.60 (SD 0.6)	17.0 (SD 2.9)	44 (n = 63)
2012	36.4 (SD 0.4)	36.0 (SD 0.5)	117.7 (SD 27.2)	- 0.46 (SD 0.5)	17.1 (SD 2.5)	45.5 (n = 66)
2013	36.3 (SD 0.4)	35.8 (SD 0.6)	109.0 (SD 23.2)	- 0.59 (SD 0.5)	16.2 (SD 2.5)	43 (n = 30)
2014	36.2 (SD 0.6)	36.0 (SD 0.6)	(Insufficient numbers)	0.15 (SD 1.1)	17.0 (SD 2.7)	52 (n = 5)
P value	0.06	0.01*	< 0.001**	0.172	0.014*	0.006**

* significance < 0.05
** significance < 0.01

Table 6: Temperature outcomes: emergency and elective patients

Temperature outcome	Category		Significance
	Emergency	Elective	
Mean preoperative temperature (°C)	36.4 (SD 0.5)	36.5 (0.5)	0.4
Mean PACU arrival temperature (°C)	36.0 (SD 0.6)	35.8 (SD 0.5)	0.001**
Postoperative hypothermia	80 (48%)	121 (64%)	0.03*
Temperature decline: preoperative temperature to PACU arrival (°C)	-0.53 (SD 0.6)	-0.69 (SD 0.6)	0.03*
Pregnancy-induced hypertension (PIH)	26 (15.6%)	6 (3.2%)	0.001**

* significance < 0.05
** significance < 0.01

Appendix P

Randomised controlled trial

Mater Human Research Ethics Committee, Queensland University of Technology and Mater Research Governance Approvals

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17 September 2014

Judy Munday
Nursing Research Centre
Mater Health Services

Dear Judy

HREC Ref N°: HREC/14/MHS/157
Project title: A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

I refer to your letter dated 25 July 2014. This application was considered by the Mater Health Services Human Research Ethics Committee (MHS HREC) (EC00332) at its meeting of 19 August 2014 and your responses were further reviewed at the 16 September 2014 meeting.

I am pleased to advise you that the MHS HREC has granted ethical approval of this application.

*In all future correspondence with the Research Ethics Office please quote the Mater reference number **HREC/14/MHS/157.***

The nominated participating site/s in this project is/are:

- Mater Health Services

The approved documents include:

Document	*Version*	*Date*
NEAF Application Submission Code AU/1/B9B9110	2.2 (2014)	25 July 2014
Covering Letter	1	25 July 2014
Investigator CV: CV Supervisor CV (Patsy Yates)	1	25 July 2014
Investigator CV: Associate Investigator CV (David Sturgess)	1	25 July 2014
Investigator CV: Associate Investigator CV (Sonya Osborne)	1	25 July 2014
Investigator CV: CV - Judy Munday (Principal Investigator)	1	24 July 2014
Covering Letter for response to further information - ***Noted***	2	09 September 2014
Response to Request for Further Information - ***Noted***		09 September 2014
Protocol	V2	09 September 2014
Letter of Invitation to participant	V2	09 September 2014

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research (2007), updated in 2014. The processes used by this HREC to review multi-centre research proposals have been certified by the National Health and Medical Research Council.

Mater Research HREC Office
Room 294 Level 2 Aubigny Place *Ph: 07 3163 1585 Fax: 07 3163 1588* *Email: research.ethics@mmri.mater.org.au*

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Consent Form	V2	01 September 2014
Data Collection Tool	V2	09 September 2014
Participant Information Brochure	V2	01 September 2014

This letter constitutes ethical approval only. This research cannot proceed until separate Research Governance authorisation has been obtained from the Chief Executive Officer or Delegate of the institution under whose auspices the research will be conducted. Please note it is a requirement that the approved documents as listed above are provided to the Research Governance Office. In this regard, please contact Dr Louise Hutley, Senior Research Governance Officer on 3163 8836 for assistance.

Approval of this project by the MHS HREC is valid from 17 September 2014 to 17 September 2017, subject to the following conditions being met:

- The Principal Investigator will immediately report anything that might warrant review of ethical approval of the project.
- The Principal Investigator will notify the MHS HREC of any event that requires a modification to the protocol or other project documents and submit any required amendments.
- The Principal Investigator will submit any necessary reports related to the safety of research participants.
- In accordance with *Section 3.3.22(b)* of the National Statement the Principal Investigator will report to the MHS HREC annually, the first report being due on 16 September 2015 and a final report is to be submitted on completion of the study.
- The Principal Investigator will notify the MHS HREC if the project is discontinued before the expected completion date, with reasons provided.
- The Principal Investigator will notify the MHS HREC of any plan to extend the duration of the project past the approval period listed above and will submit any associated required documentation.

Please confirm the commencement date with the Research Ethics Office.

Should you have any queries about the MHS HREC's consideration of your project, please contact the HREC Coordinator on (07) 3163 1585. The MHS HREC Terms of Reference, membership and standard forms are available at *http://www.mater.org.au/Home/Research/Human-Research-Ethics-Committee/Human-Research-Ethics/HREC-Resources)*

The MHS HREC wishes you every success in your research.

Yours sincerely

Ms Madonna McGahan
Acting Chairperson
Mater Health Services Human Research Ethics Committee

University Human Research Ethics Committee (UHREC)

HUMAN RESEARCH ETHICS APPROVAL CERTIFICATE

NHMRC Registered Committee Number EC00171

Date of Issue: 30/6/16 (supersedes all previously issued certificates)

Dear Dr Sonya Osborne

This approval certificate serves as your written notice that the proposal has met the requirements of the *National Statement on Ethical Conduct in Human Research* and has been approved on that basis. You are therefore authorised to commence activities as outlined in your application, subject to any specific and standard conditions detailed in this document.

Project Details

Category of Approval: Administrative Review

Approved From: 4/11/2014 **Approved Until:** 17/09/2017 (subject to annual reports)

Approval Number: 1400000742

Project Title: A preoperative warming regime versus no preoperative warming for maintenace of normothermia in women receiving intrathecal morphine for caesarean section

Investigator Details

Chief Investigator: Dr Sonya Osborne

Other Staff/Students:

Investigator Name	Type	Role
Mrs Judy Munday	Student	Doctoral (Research)
Dr David Sturgess	External	External Associate Supervisor
Prof Patsy Yates	Internal	QUT Associate Supervisor

Conditions of Approval

Specific Conditions of Approval:
As per Mater Health Services Human Research Ethics Committee

Standard Conditions of Approval:

1. Conduct the project in accordance with QUT policy, the ***National Statement on Ethical Conduct in Human Research*** (http://www.nhmrc.gov.au/guidelines/publications/e72), the ***Australian Code for the Responsible Conduct of Research*** (http://www.nhmrc.gov.au/guidelines/publications/r39), any associated legislation, guidelines or standards;
2. Gain UHREC approval for any proposed variation (http://www.orei.qut.edu.au/human/var/) to the project **prior** to implementation;
3. Respond promptly to the requests and instructions of UHREC;
4. Declare all actual, perceived or potential conflicts of interest;
5. Immediately advise the Office of Research Ethics and Integrity (http://www.orei.qut.edu.au/human/adv/) if:
   - any unforeseen development or events occur that might affect the continued ethical acceptability of the project;
   - any complaints are made, or expressions of concern are raised, in relation to the project;
   - the project needs to be suspended or modified because the risks to participants now outweigh the benefits;
   - a participant can no longer be involved because the research may harm them; and
6. Report on the progress of the approved project at least annually, or at intervals determined by UHREC. The Committee may also choose to conduct a random audit of your project.

If any details within this Approval Certificate are incorrect please advise the Research Ethics Unit within 10 days of receipt of this certificate.

End of Document

MHS & MMRI Human Research Governance - SSA Authorisation

8 December 2014

Mrs Judy Munday
Clinical Research Nurse
Mater Nursing Research Centre
Room 284, Level 2 Aubigny Place, Raymond Terrace
South Brisbane QLD 4101

Dear Mrs Munday

Re: Mater Research Governance Ref. RG-14-338
HREC Reference Number: HREC/14/MHS/157
Project Title: A preoperative warming regime for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Thank you for submitting an application for authorisation of this project. I am pleased to inform you that authorisation has been granted for this study to take place at the following site(s):

Mater Mothers' Hospital and Mater Research, South Brisbane

Documents reviewed and Authorised by Mater Research Governance are as per HREC Approval Letters dated 17 September 2014 and 4 December 2014 and include:

- *Protocol; Version 2 dated 9 September 2014*
- *Participant Information Brochure; Version 3 dated 3 November 2014*

The following conditions apply to this research proposal. These are additional to those conditions imposed by the Human Research Ethics Committee that granted ethical approval.

1. The Research Governance Officer must be informed of any problems that arise during the course of the study which may affect conduct of the study at the site.
2. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project, and which are submitted to the HREC for review, are copied to the research governance officer;

Head office
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3. Proposed amendments to the research protocol or conduct of the research which only affects the ongoing site acceptability of the project, are to be submitted to the research governance officer;
4. Proposed amendments to the research protocol or conduct of the research which may affect both the ongoing ethical acceptability of the project and the site acceptability of the project are to be submitted to the research governance officer after a HREC decision is made.

We wish you every success in undertaking this research.

Yours sincerely

Dominique Rossouw
Research Governance Officer
Mater Research Office
Room 270, Lvl 2, Aubigny Place, Raymond Terrace
South Brisbane Qld 4101
Email address: research.governance@mmri.mater.org.au

Appendix Q

Randomised controlled trial

Participant Information and Consent Forms

Participant Information Brochure

Title:	A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.
Principal Investigator:	Judy Munday (Affiliations: Mater Health Services, Queensland University of Technology)
Associate Investigators:	Dr David Sturgess (Affiliation: Mater Health Services), Dr Simon Maffey (Affiliation: Mater Health Services), Dr Sonya Osborne (Affiliation: Queensland University of Technology, Professor Patsy Yates: Queensland University of Technology).
Location:	Mater Mother's Hospital Operating Theatres

Part One What does my participation involve?

1. Introduction

We would like to invite you to participate in this research study. You are eligible to participate in this study because you are being admitted for an elective caesarean section at the Mater Mother's Hospital. This study aims to test a regime to keep women warm whilst they are undergoing caesarean section and reduce the amount of temperature decline that they experience.

This Participant Information Brochure tells you about the research project. This information aims to help you decide whether or not you would like to take part in the research.

Please read the information provided carefully. Please also ask questions about anything that you don't understand or want to know more about. You can also discuss this with someone else before deciding whether to take part.

Participation in the study is entirely voluntary – you do not have to take part if you do not want to. You will still receive the best possible care whether you take part or not. It is also important to consider that your participation also involves your unborn baby.

If you do decide to take part in the research project, you will be asked to sign the Consent Form. If you sign this, you are confirming that you understand what you have read, provide consent to take part in the project, consent to have treatments that are described and consent to the use of your personal and health information as described. A copy of this Participant Information Brochure, along with the Consent Form, will be given to you.

2. What is the purpose of this research?

The overall aims of the research study are to improve methods of temperature management that we provide to women undergoing caesarean section and reduce the incidence of heat loss during and after surgery.

It is recognized that many women undergoing caesarean section experience a reduction in their temperature and some will experience mild perioperative hypothermia (that is, heat loss or a low body temperature directly related to undergoing a surgical procedure). It is also known that this can cause other complications, along with discomfort. Research suggests that some women who receive a dose of morphine into their spine for pain relief during caesarean section, experience lower body temperatures. Providing warming to patients before surgery has been shown to be effective in other patient groups, but it is unknown if this is effective when women are receiving spinal morphine for caesarean section.

To develop more effective methods of keeping women warm whilst they undergo caesarean section we plan to test the effectiveness of a warming regime to maintain body temperature. It is hoped that this research will improve the care we provide for women in terms of their temperature management in theatre, and improve their experience of caesarean section.

Medications, drugs and devices have to be approved for use by the Australian Federal Government. The Cocoon™ warming device used in this study is approved in Australia for patient warming.

The results of this research will be used by the primary investigator (Judy Munday) to obtain a Doctor of Philosophy (PhD) degree.

3. What does participation in this research involve?

You will need to have time to read the participant information brochure and ask any questions that you have, before signing the consent form. The research assistant or primary investigator will then conduct further screening of your medical history to ensure that you are eligible to participate, as some pre-existing conditions may have an effect on the appropriateness of the intervention, for example thyroid disorders (as they may affect the way that the body controls temperature), vascular disease or a known allergy to morphine.

You will be participating in a randomised controlled research project. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). Depending on the theatre schedule, you may or may not be approached to take part in the study on the day of surgery Also on the day of surgery the principal investigator will assess whether you are still eligible to take part – for example, if you have developed a high body temperature on the day of surgery or had developed high blood pressure then you would not be able to take part in the study. As temperature measurements will be taken via the ear canal (as is usual practice), to ensure accuracy of this reading for this study, all participants in the study will also receive otoscopy – that is, inspection of the ear canal – on the day of surgery. Participants in this research project will be assigned to one of two groups. One group will receive the warming regime, whilst the other group will receive usual care. Participants will be randomly assigned to one of the two groups. There is a one in two chance of receiving the intervention under investigation.

Once randomization has been carried out, the research assistant or principal investigator will collect some basic information about you, such as your age, height, weight and the number of babies and pregnancies you have had.
If assigned to the control group you will not receive the preoperative warming intervention. You will be asked to wear hospital gown, dressing gown and slip-on footwear, as is normal procedure. You will be transferred to the Preoperative Waiting Area approximately 30 minutes before your expected procedure time. If you become cold, warmed blankets will be provided. After the anaesthetic is given, a warmed blanket will be wrapped around you.
If in the intervention group you will also be asked to wear hospital gown, dressing gown and slip-on footwear, as is normal procedure. You will be transferred to the Preoperative Waiting Area approximately 30 minutes before your expected procedure time. Whilst awaiting surgery a warming blanket will be applied that uses warm air – the duration of this procedure will be 20 minutes. After the anaesthetic is given, a warmed blanket will be wrapped around you. If changes to theatre scheduling arise that involve a longer waiting period between the application of the warming and the commencement of surgery, then this may mean that your data will not be included in the study and for the remainder of the procedure you will then receive standard care.
Both groups will receive temperature measurements when they arrive in the Preoperative Waiting Area and at further regular intervals throughout the waiting period, through surgery and in the Post Anaesthetic Care Unit. In the Preoperative Waiting Area and in the Post Anaesthetic Care Unit these measurements will be taken using a thermometer which is inserted into your ear canal, which is usual practice. Whilst in the operating theatre, your temperature will also be measured via the urinary catheter which you receive as part of normal care The principal investigator will be responsible for recording the temperature measurements and also other information including the duration of the operation and blood loss. The temperature at birth, and Apgar scores, of your baby are routinely collected for normal clinical care: these will also form part of the data collection for the study. The primary investigator will be present throughout the operation and the recovery period in the Post Anaesthetic Care Unit, until you are transferred to the ward for further recovery. Information about feeding, skin-to-skin contact and wound infection both in hospital and postnatally is routinely collected as part of your normal care: this data will also form part of the data collection for this study.
This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study investigators or participants jumping to conclusions.
There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

4. Other relevant information about the research project
In total 50 people will be taking part in the project overall. This is a single-site study and is only being run at the Mater Mother's Hospital.

5. Do I have to take part in this research project?
Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.
If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.
Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Mater Mother's Hospital.

6. What are the alternatives to participation?
You do not have to take part in this research project to receive treatment at this hospital. Other options are available; these include receiving usual care. Usual care provided does not include the use of a warming regime using a warm air blanket whilst waiting for surgery, however warmed cotton blankets are available at any stage if you feel cold.

7. What are the possible benefits of taking part?
We cannot guarantee or promise that you will receive any benefits from this research; this research will benefit patients in the future by helping us to develop warming regimes that are suitable for women undergoing caesarean section and reduce rates of heat loss in women

8. What are the possible risks and disadvantages of taking part?
Treatments often cause side effects. You may have none, some or all of the effects listed below. If you have any of these side effects please talk with the investigators. The investigators and research assistants will also be looking out for side effects.
The warming device used is already in use in Mater Mother's Hospital, however it is usually used during and after surgery rather than before. Possible side effects from the forced air warming blanket may include, in some people, feeling too hot, or sweating – if this occurs the research assistant will cease the warming. Where procedures regarding the use of the forced air warming blanket have been incorrectly followed, and the hose has not been connected to the blanket correctly, there have been reported cases of thermal burns, however this is extremely rare and unlikely. This study follows a strict procedure to ensure safe usage of this device, which is already in use in the study hospital for patient warming.
If any of the above symptoms commence during warming then the warming blanket will be removed and appropriate care provided to you to make you more comfortable.

9. What if new information arises during this research project?
Sometimes during the course of a research project, new information becomes available out the treatment that is being studied. If this happens, the investigator will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw from either group, the investigator will make arrangements for your regular health care to continue, without any further data collected. Also, on receiving new information, the investigator might consider it to be in your best interest to withdraw you from the research project. If this happens she will explain the reasons and arrange for your regular health care to continue.

10. Can I have other treatments during this research project?
You can receive all other care, medications and treatments as normal during this research project. No treatments or medications need to be stopped for the time you are involved in the research project.

11. What if I withdraw from this research project?
If you decide to withdraw from the project, please notify a member of the research team before you withdraw. If you do withdraw your consent during the research project, the investigator and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

12. Could this research project be stopped unexpectedly?
The research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The treatment was not shown to be effective
- The treatment was shown to work and did not need further testing

13. What happens when the research project ends?

It is anticipated that the outcomes of this research will be finalised by June 2015. It is also intended that the outcomes of the research will be published by the investigators. If you would like to receive feedback or information regarding the success of the project, please indicate by ticking the box on the consent form.

Part Two How is the research project being conducted?

1. What will happen to information about me?

By signing the consent form you consent to the relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. No names will be used. The data will only be accessible by the researchers and will be kept in a locked cabinet and in a password projected computer file at Mater Health Services and then destroyed in accordance with legal requirements. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.
Any information obtained during the research project and your health records are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities, Mater Health Services, the institution relevant to this Participant Information Brochure, or as required by law. By signing the Consent Form, you authorize release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.
It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified and results will be

collated. Information about your participation in this research project may be recorded in your health records.
In accordance with relevant and /or Queensland privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. Please contact the study team member named at the end of this document if you would like to access your information.
Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will only be disclosed with your permission, or as required by law.

2. Complaints

If you suffer any injuries or complications as a result of this research project, you should contact the research team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital. If you have concerns regarding the research you may contact the Principal Investigator, Judy Munday, on mobile 0406721314 or 07 3163 5368 (Mater Nursing Research Centre). If you have any concerns regarding your care at Mater Mother's Hospital please contact the Mater Mother's Patient Liaison Officer (details below).

3. Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Mater Health Services and Queensland University of Technology.
The research will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

4. Further information and who to contact

The person you may need to contact will depend on the nature of your query.
If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study investigator Judy Munday on 0406721314. Alternatively you may contact the Clinical Contact Person listed below:

Clinical Contact Person

Name	**Dr Simon Maffey.**
Position	Deputy Director – Obstetric Anaesthesia
Telephone	3163 8646
Email	**Simon.maffey@mater.org.au**

Primary Supervisor

This study is being conducted as part of a PhD program. The contact details for the Primary Supervisor for the Principal Investigator (Judy Munday) are as follows:

Name	**Dr Sonya Osborne**
Position	**Senior Lecturer**
Telephone	3138 3785
Email	**s.osborne@qut.edu.au**

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints Contact Person

Name	Roxanne Regan
Position	Patient representative
Telephone	3163 8303
Email	Roxanne.Regan@mater.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Mater Health Services
HREC Executive Officer	HREC Coordinator
Telephone	3163 2392
Email	research.ethics@mmri.mater.org.au

Consent Form

Title:	A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.
Principal Investigator:	Judy Munday (Affiliations: Mater Health Services, Queensland University of Technology
Associate Investigators:	Dr David Sturgess (Affiliation: Mater Health Services), Dr Sonya Osborne (QUT), Professor Patsy Yates (QUT)
Location:	Mater Mother's Hospital Operating Theatres

Declaration by participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for the use of my personal information for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

I would like to receive feedback on the outcomes of the study: Yes ☐ o If y ☐ please provide preferred contact details below to enable us to provide you with feedback:

Contact details for feedback:

Name of participant (please print):

Signature:_____ Date:

Under certain circumstances (see Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 at 4.8.9) a witness* to informed consent is required.

Declaration by Senior Researcher

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Senior Researcher[#] (please print):
Signature: Date:

[#] A senior member of the research team must provide the explanation of, and information concerning, the research project.
Note: All parties signing the consent form must date their own signature

Appendix R

Randomised controlled trial

Intraoperative and Anaesthetic Protocol

Intraoperative Protocol

Exclusions prior to randomisation for the following:

Planned avoidance of intrathecal morphine use: for example, morphine allergy, planned epidural top-up, planned general anaesthetic
Non-elective CS
Planned ICU admission post-op
Known altered thermoregulation: previous or current thyroid disorder requiring surgery or medical therapy
Vascular disease or poor cutaneous perfusion
Aural canal not visible on otoscopy
Inability to apply preoperative warming strategy or admission temperature ≥ 37°C
ASA score >II
History of preeclampsia or eclampsia
Clinician declined patient involvement.

Exclusions after randomisation for the following:

CSE with opioids via epidural catheter
CSE with > 10mls of local anaesthetic via epidural catheter
Delay between completion of warming intervention and the transfer to theatre >20 minutes.
Any other deviation from stated intraoperative protocol (see below)

Spinal anaesthetic protocol

Spinal anaesthetic technique:	spinal (or CSE with no opioids via epidural catheter)
Kit/equipment:	any
Spinal local anaesthetic:	heavy 0.5% bupivacaine 1.8-2.5mls
Spinal morphine:	100mcg
Spinal fentanyl:	15-20mcg
CSE epidural local anaesthetic (if used):	1% ropivicaine ≤ 10mls

Additional medication

Vasopressor
Antibiotic
Anti-emetic
Analgesia: Paracetamol 1g PR, Diclofenac 100mg PR
Oxytocic: Carbetocin 100mg
Additional (as required)

Fluids (< 2 litres) via Biegler Fluid Warmer at 38.5°C

Solution	Additive	Time Commenced	VolumeRate

Intraoperative Warming

Blankets (warmed): ≤ 2
IV Fluid warming (as above): 38.5°C via Biegler fluid warmer

Temperature Monitoring

Mon-a-Therm™ foley catheter bladder temperature measurements
Aural canal (tympanic) Genius™ thermometers

Appendix S

Randomised controlled trial

Data Collection Tool

A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Participant Demographic Data Collection Form

Study ID No: ☐ Date: ☐

5. Age
6. Parity
7. Gravidity
8. Pre-pregnancy BMI:

A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Preoperative Intervention / Control Data Collection (to be detached from Outcome Measurement Form)

Study ID No: ☐

Patient attire (tick all that apply)

Surgical gown ☐ Dressing gown Footwear ☐

Maternal thermal comfort *recorded on separate outcomes measurement form

Preoperative Maternal temperature *recorded on separate outcomes measurement form

Preoperative Warming Protocol (FOR INTERVENTION GROUP ONLY)

Blanket size: ☐

Time Preoperative Warming Commenced: ☐

Setting: ☐

Time Preoperative Warming Ceased: ☐

Further information (please tick all that apply and provide further information):

Warming ceased early

If yes, reason ☐

Nausea ☐ Further info ☐

Vomiting ☐ Further info ☐

Sweating ☐ Further info ☐

Other ☐ Further info ☐

Temperature (°C) at 10 mins:

Ambient Temp (°C):

A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Anaesthetic and Intraoperative Data Collection

Study ID No

Preoperative medication

ASA score

Spinal Anaesthetic Information

Position

Procedure

Level

Needle

Local anaesthetic and volume

Opioids

Block level

Reinsertion

Additional medication

Vasopressor

Antibiotic

Anti-emetic

Analgesia

Oxytocic

Additional

Fluids

Solution	Additive	Time Commenced	Volume	Rate

Warming

Blankets

IV Fluid warming

IV Fluid warming method

Temperature Monitoring

Details

A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Outcomes Measurement

Study ID No

Maternal Temperature				
Timepoint	Actual Time	Temperature (°C)	Measurement device	Comments
Baseline*				
Pre-spinal				
Post-spinal				
OT: 15 mins Aural				
IDC				
OT: 30 mins Aural				
IDC				
OT: 45 mins Aural				
IDC				
OT: 60mins Aural				
IDC				
OT: 90mins Aural				
IDC				
OT: end of procedure Aural				
IDC				
PACU arrival				
PACU: 15 mins				
PACU: 30 mins				
PACU: 45 mins				
PACU: 60 mins				
PACU: ready for discharge				

Mean Arterial Pressure (MAP) (mmHg)	
Baseline	
Pre-spinal	
Post-spinal	
OT:end of procedure	

Maternal Thermal Comfort (via 100mm Visual Analogue Scale)	
Baseline	
Pre-spinal	
OT:end of procedure	
PACU: 30 mins	

Maternal Shivering		
0= no shivering, 1= mild, intermittent shivering, 2= intense, continuous shivering[1]		
Baseline		
Pre-spinal		
OT:end of procedure		
PACU: arrival		
PACU: 15 mins		
PACU: 30 mins		
Therapies administered for shivering		
Time	Therapy	Outcome

A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Study ID No

Intraoperative Data		
Outcome		Comments
Intraoperative blood loss (mls)		
Intravenous fluid infusion volume (mls)		
Procedure duration (mins): knife to skin to end procedure		
Ambient Temp (°C):		

Neonatal Data		
Outcome		Comments
Apgar 1 minute		
Apgar 5 minutes		
	(°C)	Route
Temperature at birth (°C)		

Neonatal Data – adverse events			
Outcome			Comments
Admission to ICN? (circle)	Yes	No	
Admission to SCN? (circle)	Yes	No	
	(mmols)	Time	Comments
Blood sugar (if applicable)			
	Comments / intervention		
Respiratory distress			

Adverse Events (if applicable)			
Event	Time	Comments	Outcome (eg withdrawal)

Deviations from protocol (if applicable)		
Event	Time	Comments

A preoperative warming regime versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean section.

Study ID No ☐

Breastfeeding and Skin-to-skin	
Skin-to-skin at birth	Not at all ☐ Up to 15 mins ☐ 15-30 mins ☐ 34-45mins ☐ 45-60 mins ☐ >60mins ☐ N/A ☐
Infant feeding intention at birth	Breastfeeding ☐ Breastfeeding & EBM* ☐ EBM ☐ Breastfeeding & Formula ☐ Formula ☐ N/A ☐ Not known ☐
Feeding at birth	Breastfeeding ☐ EBM ☐ Breast milk & Formula ☐ No feed given ☐ N/A ☐ Other ☐
Timing of feed (how soon after birth)	15 min ☐ 30 min ☐ 45 min ☐ 60 min ☐ 1-2hrs ☐ 2 hrs ☐ > 2hrs ☐ Not known ☐ N/A ☐
Universal Postnatal Contact : Feeding	Breastfeeding ☐ Suppressing Lactation ☐

Wound Infection			
Event			Comments
Wound infection on discharge	Yes	No	
Management: antibiotics (if applicable)?	Yes	No	
Wound dehiscence on discharge	Yes	No	Management (if applicable): Antibiotics ☐ Return to OT ☐ Wound dressing ☐ Other/comment:
Universal Postnatal contact: Caesarean wound concerns?	Yes	No	Comments:

Postoperative warming (if applicable)		
Method	Time	Comments

Study ID No [ ]

Thermal Comfort

Please circle the place on the scale that best describes your level of thermal comfort (how warm or cool you feel).

Baseline

0 1 2 3 4 5 6 7 8 9 10

Worst Imaginable cold **Comfortable** **Insufferably hot**

Pre-spinal

0 1 2 3 4 5 6 7 8 9 10

Worst Imaginable cold **Comfortable** **Insufferably hot**

OT: end of procedure

0 1 2 3 4 5 6 7 8 9 10

Worst Imaginable cold **Comfortable** **Insufferably hot**

Appendix T

Randomised controlled trial

Per protocol analysis

Pre-operative warming versus no preoperative warming for maintenance of normothermia in women receiving intrathecal morphine for caesarean delivery: a single-blinded, randomised controlled trial.

Per-protocol analysis

The per-protocol population excluded participants who had not received the entire 20 minute warming intervention, or had been exposed to other deviations from the stated protocol, such as an extended duration between the intervention and commencement of surgery.

Results

Per-protocol analysis indicated a statistically significant difference in temperature change from baseline to end of procedure in favour of active preoperative warming: F (1,34) = 5.42, p = 0.03, partial eta squared = 0.14 (see Table 1).

The lowest individual intraoperative temperature of 34.7°C was experienced at 15 minutes after spinal anaesthesia by a single patient in the control group, while the lowest individual intraoperative temperature experienced by a patient in the pre-operative warming group was 35.1°C at 45 minutes post spinal anaesthesia, in the ITT population. When considered using per-protocol analysis, the nadir temperature for the control group remained the same, however the lowest individual intraoperative temperature in the pre-operative warming group was 35.4°C at 30 minutes post spinal anaesthesia.

Table 1: Temperature change (°C): baseline-end of procedure and hypothermic patients at each time point

	Temperature change °C (baseline – end of procedure): mean (SD) number		
	Intervention	**Control**	**P value**
Intention-to- treat	0.5 (SD 0.32) (n=25)	0.7 (SD 0.57) (n=25)	0.28
Per-protocol	0.4 (SD 0.27) (n=18)	0.8 (SD 0.43) (n=19)	0.03

Appendix U

Randomised controlled trial

Statement of Contributions (Submitted paper)

Statement of Contribution of Co-Authors for Thesis by Published Paper

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student's thesis and its publication on the Australasian Research Online database consistent with any limitations set by publisher requirements.

In the case of this chapter:

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Contributor	**Statement of contribution***
Student author: Judy Munday Signature: Munday Date: 7th January 2017	Developed the research protocol, and study design, collected data, conducted data analysis, and wrote the final manuscript. I am the principal author based on the International Committee of Medical Journal Editors criteria for authorship.
Co-author: Dr Sonya Osborne	Assisted in development of protocol, aided study design and reviewed final manuscript.
Co-author: Professor Patsy Yates	Assisted in development of protocol, aided study design, and reviewed of final manuscript.
Co-author: Dr David Sturgess	Assisted in study design, development of anaesthetic protocol, and review of final manuscript.
Co-author: Lee Jones	Assistance in data analysis plan, review of data analysis and review of final manuscript.
Co-author: Edward Gosden	Assisted in protocol development, data analysis plan, review of data analysis and review of final manuscript.

Principal Supervisor Confirmation:
I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name: Sonya Osborne Signature Sosborne Date 16/1/2017